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* * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *


FILE 'HOME' ENTERED AT 13:55:33 ON 26 MAR 2003

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 13:55:40 ON 26 MAR 2003

=> e lysosomal acid lipase/cn
E1            1     LYSOSOMAL .ALPHA.-MANNOSIDASE (HUMAN HELA CELL PRECURSOR RED
                    UCED)/CN
E2            1     LYSOSOMAL .ALPHA.-N-ACETYLGLUCOSAMINIDASE/CN
E3            1 --> LYSOSOMAL ACID LIPASE/CN
E4            1     LYSOSOMAL ACID LIPASE (ARABIDOPSIS THALIANA GENE AT2G15230)/
                    CN
E5            1     LYSOSOMAL ACID LIPASE (HUMAN 280-AMINO ACID FRAGMENT)/CN
E6            2     LYSOSOMAL ACID LIPASE (HUMAN)/CN
E7            1     LYSOSOMAL ALPHA-MANNOSIDASE (HUMAN GENE MANB)/CN
E8            1     LYSOSOMAL AMINO ACID TRANSPORTER 1 (RAT STRAIN SPRAGUE-DAWLE
                    Y)/CN
E9            1     LYSOSOMAL CARBOXYPEPTIDASE B/CN
E10           1     LYSOSOMAL ENZYME ACETYLGLUCOSAMINE-1-PHOSPHOTRANSFERASE/CN
E11           1     LYSOSOMAL ENZYME N-ACETYLGLUCOSAMINE-1-PHOSPHOTRANSFERASE/CN
E12           1     LYSOSOMAL ENZYME PRECURSOR ACETYLGLUCOSAMINE-1-PHOSPHOTRANSF
                    ERASE/CN

=> s e3
L1            1 "LYSOSOMAL ACID LIPASE"/CN

=> d

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   9026-00-0  REGISTRY
CN   Esterase, cholesterol (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Bile salt-stimulated lipase
CN   Cholesterase
CN   Cholesterin esterase
CN   Cholesterol ester hydrolase
CN   Cholesterol esterase
CN   Cholesteryl ester hydrolase
CN   Cholesteryl esterase
CN   COE 311
CN   E.C. 3.1.1.13
CN   Lysosomal acid lipase
CN   Neutral cholesteryl ester hydrolase
CN   Sterol ester hydrolase
CN   Sterol esterase
DR   9040-56-6
MF   Unspecified
CI   MAN
LC   STN Files:   AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,
       CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, EMBASE,
       IFICDB, IFIPAT, IFIUDB, PROMT, TOXCENTER, USPAT2, USPATFULL
     Other Sources:   EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            1721 REFERENCES IN FILE CA (1962 TO DATE)
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            22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          1722 REFERENCES IN FILE CAPLUS (1962 TO DATE)


=> set expand cont
SET COMMAND COMPLETED

=> sel l1 name
E13 THROUGH E25 ASSIGNED

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     6.99       7.20

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS,
       BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT,
       CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE,
       DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 13:56:51 ON 26 MAR 2003

66 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s e13-25 (l)(atheroscleros? or arterioscleros?)
           2   FILE ADISCTI
           1   FILE ADISINSIGHT
           4   FILE AGRICOLA
   8 FILES SEARCHED...
          83   FILE BIOSIS
           5   FILE BIOTECHABS
           5   FILE BIOTECHDS
          20   FILE BIOTECHNO
  12 FILES SEARCHED...
          11   FILE CABA
           6   FILE CANCERLIT
         129   FILE CAPLUS
  17 FILES SEARCHED...
           1   FILE CIN
          12   FILE DDFB
           7   FILE DDFU
  23 FILES SEARCHED...
           4   FILE DGENE
  24 FILES SEARCHED...
          12   FILE DRUGB
           3   FILE DRUGNL
          14   FILE DRUGU
           2   FILE DRUGUPDATES
  31 FILES SEARCHED...
          63   FILE EMBASE
          24   FILE ESBIOBASE
  33 FILES SEARCHED...
           8   FILE FEDRIP
           1   FILE FROSTI
           3   FILE IFIPAT
  41 FILES SEARCHED...
          31   FILE JICST-EPLUS
           2   FILE LIFESCI
          65   FILE MEDLINE
  47 FILES SEARCHED...
          27   FILE PASCAL
  51 FILES SEARCHED...
           1   FILE PHAR
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          3   FILE PHIN
          2   FILE PROMT
         62   FILE SCISEARCH
  58 FILES SEARCHED...
         28   FILE TOXCENTER
        189   FILE USPATFULL
  61 FILES SEARCHED...
          6   FILE USPAT2
         35   FILE WPIDS
  65 FILES SEARCHED...
         35   FILE WPINDEX

  36 FILES HAVE ONE OR MORE ANSWERS,    66 FILES SEARCHED IN STNINDEX

L2    QUE ("BILE SALT-STIMULATED LIPASE"/BI OR CHOLESTERASE/BI OR "CHOLESTERIN E
          STERASE"/BI OR "CHOLESTEROL ESTER HYDROLASE"/BI OR "CHOLESTEROL ESTERA
          SE"/BI OR "CHOLESTERYL ESTER HYDROLASE"/BI OR "CHOLESTERYL ESTERASE"/B
          I OR "COE 311"/BI OR "E.C. 3.1.1.13"/BI OR "LYSOSOMAL ACID LIPASE"/BI
          OR "NEUTRAL CHOLESTERYL ESTER HYDROLASE"/BI OR "STEROL ESTER HYDROLASE
          "/BI OR "STEROL ESTERASE"/BI) (L)(ATHEROSCLEROS? OR ARTERIOSCLEROS?)

=> s l2(L)(treat? or therap?)
          2   FILE ADISCTI
          1   FILE ADISINSIGHT
    4 FILES SEARCHED...
         16   FILE BIOSIS
          3   FILE BIOTECHABS
   10 FILES SEARCHED...
          3   FILE BIOTECHDS
          2   FILE BIOTECHNO
          1   FILE CABA
   13 FILES SEARCHED...
          2   FILE CANCERLIT
         22   FILE CAPLUS
   16 FILES SEARCHED...
          1   FILE DDFB
          3   FILE DDFU
          4   FILE DGENE
   24 FILES SEARCHED...
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          3   FILE DRUGNL
         10   FILE DRUGU
         19   FILE EMBASE
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          4   FILE FEDRIP
   34 FILES SEARCHED...
          1   FILE FROSTI
          3   FILE IFIPAT
   41 FILES SEARCHED...
          3   FILE JICST-EPLUS
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   44 FILES SEARCHED...
         19   FILE MEDLINE
   50 FILES SEARCHED...
          4   FILE PASCAL
   52 FILES SEARCHED...
          1   FILE PHAR
          2   FILE PHIN
          1   FILE PROMT
         10   FILE SCISEARCH
          7   FILE TOXCENTER
   60 FILES SEARCHED...
        166   FILE USPATFULL
   61 FILES SEARCHED...
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         6   FILE USPAT2
        25   FILE WPIDS
  65 FILES SEARCHED...
        25   FILE WPINDEX

  33 FILES HAVE ONE OR MORE ANSWERS,    66 FILES SEARCHED IN STNINDEX

L3    QUE L2(L)(TREAT? OR THERAP?)

=> d rank
F1          166   USPATFULL
F2           25   WPIDS
F3           25   WPINDEX
F4           22   CAPLUS
F5           19   EMBASE
F6           19   MEDLINE
F7           16   BIOSIS
F8           10   DRUGU
F9           10   SCISEARCH
F10           7   TOXCENTER
F11           6   USPAT2
F12           5   ESBIOBASE
F13           4   DGENE
F14           4   FEDRIP
F15           4   PASCAL
F16           3   BIOTECHABS
F17           3   BIOTECHDS
F18           3   DDFU
F19           3   DRUGNL
F20           3   IFIPAT
F21           3   JICST-EPLUS
F22           2   ADISCTI
F23           2   BIOTECHNO
F24           2   CANCERLIT
F25           2   PHIN
F26           1   ADISINSIGHT
F27           1   CABA
F28           1   DDFB
F29           1   DRUGB
F30           1   FROSTI
F31           1   LIFESCI
F32           1   PHAR
F33           1   PROMT


=> file f2-12 f14-33
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               13.20      20.40

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FILE 'LIFESCI' ENTERED AT 14:11:31 ON 26 MAR 2003

FILE 'PHAR' ENTERED AT 14:11:31 ON 26 MAR 2003

FILE 'PROMT' ENTERED AT 14:11:31 ON 26 MAR 2003


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=> s l3
   1 FILES SEARCHED...
   3 FILES SEARCHED...
   5 FILES SEARCHED...
   8 FILES SEARCHED...
  10 FILES SEARCHED...
  12 FILES SEARCHED...
  16 FILES SEARCHED...
  18 FILES SEARCHED...
  20 FILES SEARCHED...
  23 FILES SEARCHED...
L4          174 L3

=> dup rem l4
DUPLICATE IS NOT AVAILABLE IN 'FEDRIP, ADISINSIGHT, PHAR'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L4
L5             92 DUP REM L4 (82 DUPLICATES REMOVED)
                  ANSWERS '1-25' FROM FILE WPIDS
                  ANSWERS '26-47' FROM FILE CAPLUS
                  ANSWERS '48-54' FROM FILE EMBASE
                  ANSWERS '55-56' FROM FILE MEDLINE
                  ANSWERS '57-62' FROM FILE DRUGU
                  ANSWERS '63-68' FROM FILE USPAT2
                  ANSWERS '69-72' FROM FILE FEDRIP
                  ANSWER '73' FROM FILE PASCAL
                  ANSWERS '74-76' FROM FILE BIOTECHDS
                  ANSWERS '77-79' FROM FILE DRUGNL
                  ANSWERS '80-82' FROM FILE IFIPAT
                  ANSWER '83' FROM FILE JICST-EPLUS
                  ANSWERS '84-85' FROM FILE ADISCTI
                  ANSWERS '86-87' FROM FILE PHIN
                  ANSWER '88' FROM FILE ADISINSIGHT
                  ANSWER '89' FROM FILE DRUGB
                  ANSWER '90' FROM FILE FROSTI
                  ANSWER '91' FROM FILE PHAR
                  ANSWER '92' FROM FILE PROMT

=> s l5(L)plaque
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L41(L)PLAQUE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
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FIELD CODE - 'AND' OPERATOR ASSUMED 'L47(L)PLAQUE'
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FIELD CODE - 'AND' OPERATOR ASSUMED 'L51(L)PLAQUE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L67(L)PLAQUE'
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FIELD CODE - 'AND' OPERATOR ASSUMED 'L69(L)PLAQUE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L75(L)PLAQUE'
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PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L81(L)PLAQUE'
  25 FILES SEARCHED...
L6   5 L5(L) PLAQUE

=> d bib abs 1-5

L6 ANSWER 1 OF 5 DRUGU COPYRIGHT 2003 THOMSON DERWENT
AN 1992-05556 DRUGU P B
TI Drugs to Treat Hyperlipidaemia.
AU Suckling K
CS SK-Beecham
LO Welwyn, United Kingdom
SO Chem.Ind.(London) (1991, No. 19, 717-22) 4 Fig. 13 Ref.
    CODEN: CHINAG ISSN: 0009-3068
AV SmithKline Beecham Pharmaceuticals, The Frythe, Welwyn, Herts, AL6 9AR, England.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 1992-05556 DRUGU P B
AB The modes of action of drugs that **treat** hyperlipidemia and **atherosclerosis** are reviewed. Current studies show that mechanisms to reduce plasma cholesterol levels can involve, 1) bile acid sequestrants (cholestyramine), 2) compounds that lower plasma triglyceride levels (nicotinic acid, acipimox and gemfibrozil), 2) HMG-CoA reductase inhibitors (lovastatin, simvastatin and pravastatin), 3) inhibitors of acyl-CoA cholesterol acyltransferase (ACAT) and **cholesteryl ester hydrolase**, enzymes which esterify cholesterol and promote its secretion into the bloodstream (Sandoz 58-035 and CL-277082), 4) antioxidants such as probucol and 5) calcium channel blockers (isradipine) which inhibit the progression of **atherosclerosis** in addition to normal antihypertensive effects.
ABEX Cholesterol, carried in the blood in lipid-protein particles (LDL) is removed from the blood largely in the liver by the uptake of LDL through a high affinity receptor, the LDL receptor. Bile acid sequestrants, anion exchange resins, work in the intestine by binding bile acids (synthesized in the liver from cholesterol) and preventing their return to the portal blood. In response to this, the liver increases its synthesis of cholesterol but also increases the level of LDL receptor expression. Nicotinic acid, acipimox and gemfibrozil lower plasma glyceride levels by affecting the secretion of triglycerides from the liver in VLDL. Earlier compounds of this type, however, have shown toxicological effects in man. HMG-CoA reductase inhibitors inhibit cholesterol synthesis at an early stage, increasing LDL receptor activity in the liver and causing a substantial clearance of LDL from the plasma. Inhibitors of ACAT and **cholesteryl ester hydrolase** provide benefits in hyperlipidemia by inhibiting the absorption of dietary and biliary secreted cholesterol, by preventing the deposition of cholesterol in the atherosclerotic **plaque** and by directing cholesterol away from the plasma compartment via inhibition of ACAT in the liver.Provided imaging techniques such as coronary angiography and B-mode ultrasound are further developed, **treatments** for **atherosclerosis** and hyperlipidemia are likely to improve dramatically. (LP)

L6 ANSWER 2 OF 5 DRUGU COPYRIGHT 2003 THOMSON DERWENT
AN 1991-33729 DRUGU T P
TI Antiatherogenic Properties of Calcium Antagonists.
AU Bond M G; Purvis C; Mercuri M
LO Winston-Salem, North Carolina, United States
SO J.Cardiovasc.Pharmacol. (17, Suppl. 4, S87-S93, 1991) 54 Ref.
    CODEN: JCPCDT ISSN: 0160-2446
AV Division of Vascular Ultrasound Research, Bowman Gray School of Medicine,

300 South Hawthorne Road, Winston-Salem, NC 27103, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 1991-33729 DRUGU T P
AB The antiatherogenic effects of calcium antagonists including lanthanum C13 (LA), azacycloheptane- 2,2-diphosphonic acid (AHDP), 2-immunopyrrolidone- 5,5-diphosphonic acid (IPDP), diltiazem (DI), flunarizine (FL), nifedipine (NI), nicardipine (NC), verapamil (VE), anipamil (AN), nilvadipine (NV), flordipine (FL), isradipine (IS) are reviewed in animals and humans **treated** with aspirin and dipyridamole. Propranolol (PR) and isosorbide dinitrate were also used. Postulated mechanisms of antiatherosclerosis retardation are reviewed. The effects of calcium antagonists cannot be explained by changes in B.P., so they must have direct effect on arterial wall processes involved in **plaque** evolution. (congress).
ABEX Calcium antagonists appear to increase clearance of accumulated LDL and cholesterol by increased binding and metabolism, and increase LDL receptor numbers and activity of lysosomal **cholesteryl ester hydrolase**. Calcium antagonists control platelet aggregation, and synthesis and release of platelet-derived growth factor. In New Zealand White rabbits (NZWRs), LA suppressed **atherosclerosis** and AHDP, IPDP and LA decreased arterial calcification and fibrosis. LA, DI and FL reduced lesions in thoracic aorta, and NI and NC inhibited **atherosclerosis** due to diet-induced hypercholesterolemia in NZWRs and Dutch belted rabbits. VE reduced cholesterol levels in the thoracic aorta in Danish strain rabbits. VE and AN had a protective effect in NZWRs. DI inhibited **atherosclerosis** and reduced aortic tissue levels of cholesterol, Ca and uronic acid in Japanese white rabbits (JWRs). NV had similar calcium channel blocking activity to NI in isolated rabbit cardiac muscle, sinus node and aortic strips, and was more potent than NI, DI and VE in inhibiting intimal thickening in JWR carotid artery. NV reduced aortic cholesterol, Ca and fat, vs. NI and NC in NZWRs. FL had no effect in NZWRs. NI reduced **atherosclerosis** in JWR but not mutant JWR lacking LDL receptors. IS inhibited matrix synthesis, and intimal thickening. LA reduced aortic cholesterol in cynomolgus monkeys.NI suppressed **atherosclerosis** in cholesterol-fed rhesus monkeys in carotid artery and thoracic aorta. NI reduced **atherosclerosis** in graft lesions of patients **treated** with aspirin and dipyridamole. NI was more protective than PR or isosorbide dinitrate against human coronary artery **atherosclerosis**. NI and NC reduced early atherosclerotic lesions. (E67/TOB)

L6 ANSWER 3 OF 5 USPAT2
AN 2001:171140 USPAT2
TI Use of mesophase-stabilized compositions for delivery of cholesterol-reducing sterols and stanols in food products
IN Akashe, Ahmad, Mundelein, IL, United States
Miller, Miranda, Arlington Heights, IL, United States
PA Kraft Foods, Inc., Northfield, IL, United States (U.S. corporation)
PI US 6376482 B2 20020423
AI US 2001-859173 20010516 (9)
RLI Division of Ser. No. US 1999-258759, filed on 26 Feb 1999
DT Utility
FS GRANTED
EXNAM Primary Examiner: Clardy, S. Mark
LREP Fitch, Even, Tabin & Flannery
CLMN Number of Claims: 41
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 1403
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Plant sterols and plant sterol esters have been shown to be

cholesterol-reducing agents in human serum. In the present invention, plant sterols, plant stanols, plant sterol esters, and plant stanol esters are incorporated into mouthfeel-enhancing, texture-building and composition-stabilizing compositions which are mesophase-stabilized compositions for use in low-fat, fat-free and triglyceride-free food products. Such compositions may be incorporated into food products resulting in low-fat, fat-free and triglyceride-free food products which may be used to deliver a recommended daily dosage of the cholesterol-reducing compounds to segments of the population which must limit it's cholesterol intake.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 4 OF 5 DRUGNL COPYRIGHT 2003 IMSWORLD

AN 95:99 DRUGNL
TI CVT 1 Moves into Phase II
SO R&D Focus Drug News (30 Jan 1995).
WC 731

L6 ANSWER 5 OF 5 IFIPAT COPYRIGHT 2003 IFI
AN 10098328 IFIPAT;IFIUDB;IFICDB
TI METHOD OF FORCING THE REVERSE TRANSPORT OF CHOLESTEROL FROM A BODY PART TO THE LIVER WHILE AVOIDING HARMFUL DISRUPTIONS OF HEPATIC CHOLESTEROL HOMEOSTASIS AND PHARMACEUTICAL COMPOSITIONS AND KIT RELATED THERETO; ADMINISTERING PHOSPHATIDE BY INJECTION
INF WILLIAMS; KEVIN JON, WYNNEWOOD, PA, US
IN WILLIAMS KEVIN JON
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG PATREA L. PABST HOLLAND & KNIGHT LLP, ONE ATLANTIC CENTER, SUITE 2000, ATLANTA, GA, 30309-3400, US
PI US 2002041894 A1 20020411
AI US 1998-71980 19980504
PRAI US 1995-5090P 19951011 (Provisional)
FI US 2002041894 20020411
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 119
GI 26 Figure(s).
FIG. 1 is a side cross-sectional view of a lipoprotein and a liposome;
FIG. 2 illustrates a table of hepatic mRNA content (pg/ mu g) for CETP, HMG-CoAR, LDL receptors, and 7a-hydroxylase; and LDL ChE;
FIGS. 3 and 4 illustrate plasma LDL cholesteryl ester concentrations in response to injections of LUVs, SUVs or saline over time in one variant:
FIG. 5 illustrates LDL receptor mRNA levels in liver in response to injections of LUVs, SUVs or saline over time;
FIG. 6 illustrates HMG-CoA reductase mRNA levels in liver in response to injection of LUVs, SUVs, or saline;
FIG. 7 Illustrates cholesteryl ester transfer protein mRNA levels in liver in response to injection of LUVs, SUVs, or saline;
FIG. 8 illustrates 7-alpha hydroxylase mRNA levels in liver in response to injections of LUVs, SUVs, or saline;
FIG. 9 illustrates key points about LUVs and atherosclerosis;
FIG. 10 illustrates plasma LDL unesterified cholesterol concentrations in response to injections of LUVs, SUVs or saline over time.
FIG. 11 illustrates plasma LDL esterified cholesterol concentrations in response to injections of LUVs, SUVs or saline over time;
FIG. 12 illustrates LDL esterified cholesterol concentrations in response to injections of LUVs, SUVs or saline;
FIG. 13 illustrates plasma VLDL esterified cholesterol concentrations in response to injections of LUVs, SUVs or saline;
FIGS. 14 and 15 illustrate HDL esterified cholesterol concentrations in response to injections of LUVs, SUVs or saline;

FIG. 16 illustrates the time course of cholesterol mobilization following an LUV injection into control or apoE KO mice;
FIG. 17 illustrates the time course of LUV clearance in control mice and apoE mice;
FIG. 18 illustrates that the compositions and methods of the present invention are effective in humans;
FIG. 19 illustrates a perspective view of an improved hemodialysis system of the present invention and improved method of hemodialysis;
FIG. 20 illustrates a perspective view of an improved peritoneal dialysis system 2000 and method of peritoneal dialysis;
FIG. 21 illustrates a perspective view of a variant of an improved peritoneal dialysis system with assaying means 2100 and method of peritoneal dialysis and analysis of spent fluid;
FIG. 22 illustrates a perspective view of an improved cardiac catheterization and/or angioplasty system 2200 and method of cardiac catheterization and/or angioplasty;.
FIG. 23 illustrates a perspective view of a variant of an improved cardiac catheterization and/or angioplasty system 2300 and method of cardiac catheterization and/or angioplasty;
FIG. 24 illustrates a graph of hepatic lipid contents in response to injections of LUVs, SUVs, or saline;
FIG. 25 illustrates plasma free cholesterol concentrations following repeated injections of SUVs or LUV (300 mg/kg) in NZW rabbits;
FIG. 26 illustrates plasma cholesterol ester concentrations following repeated injections of SUVs or LUV (300 mg/kg) in NZW rabbits;
FIG. 27 illustrates alternations in plasma components after repeated injections of SUVs; and,
FIG. 28 illustrates an agarose gel electrophoresis of whole plasma following repeated injections of LUVs, SUVs, or saline.

AB The present invention provides various methods, systems and compositions for forcing the reverse transport of cholesterol from peripheral tissues to the liver in vivo while controlling plasma LDL concentrations, and other significant components of living biological systems. The method comprises the step of parenterally administering a therapeutically effective amount of a multiplicity of large liposomes comprised of phospholipids substantially free of sterol for a treatment period whereby said liposomes pick-up said cholesterol during said treatment period. The method optionally includes the step of periodically assaying plasma LDL concentrations with an assay during said treatment period to asess said plasma LDL concentrations and obtain an LDL profile, and adjusting said parenteral administration in response to said LDL profile. Exemplary assays are selected from the group consisting of an assay of plasma esterified cholesterol, an assay of plasma apolipoprotein-B, a gel filtration assay of plasma, an ultracentrifugal assay of plasma, a precipitation assay of plasma, and a immuno turbidometric assay of plasma. Generally the compositions described herein include large liposomes of a size and shape larger than fenestrations of an endothelial layer lining hepatic sinusoids in said liver, whereby said liposomes are too large to readily penetrate said fenestrations. Therapeutically effective amounts of said compositions include in the range of 10 mg to 1600 mg phospholipid per kg body weight per dose. The large liposomes are selected from the group consisting of uni-lamellar liposomes and multi-lamellar liposomes. In variants, the liposomes have diameters larger than about 50 nm, diameters larger than about 80 nm, and diameters larger than about 100 nm. The methods optionally include the step of enhancing tissue penetration of a cholesterol acceptor by co-administration of an effective amount of a compound, said compound selected from the group consisting of a small acceptor of cholesterol and a drug that increases endogenous small acceptors of cholesterol. The small acceptor is selected from the group consisting of a high-density lipoprotein, a phospholipid protein complex having a group selected from the group consisting of apoA-I, apoA-II, apoA-IV, apoE, synthetic fragments thereof, natural fragments thereof, an amphipathic protein, and an amphipathic peptide, said protein substantially free of phospholipid, small phospholipid liposomes, and a small cholesterol acceptor. The

includes an agent that raises physiologic HDL concentrations, said agent selected from the group consisting of nicotinic acid, ethanol, a fibric acid, a cholesterol synthesis inhibitor, a drug that increases HDL concentrations, and derivatives thereof. The invention further provides a method of, and composition for regulating hepatic parenchymal cell cholesterol content and gene expression by the steps described herein. Other systems, and compositions for treating, and improving various medical techniques are also described.

CLMN 119 26 Figure(s).

FIG. 1 is a side cross-sectional view of a lipoprotein and a liposome;
FIG. 2 illustrates a table of hepatic mRNA content (pg/ mu g) for CETP, HMG-CoAR, LDL receptors, and 7a-hydroxylase; and LDL ChE;
FIGS. 3 and 4 illustrate plasma LDL cholesteryl ester concentrations in response to injections of LUVs, SUVs or saline over time in one variant:
FIG. 5 illustrates LDL receptor mRNA levels in liver in response to injections of LUVs, SUVs or saline over time;
FIG. 6 illustrates HMG-CoA reductase mRNA levels in liver in response to injection of LUVs, SUVs, or saline;
FIG. 7 Illustrates cholesteryl ester transfer protein mRNA levels in liver in response to injection of LUVs, SUVs, or saline;
FIG. 8 illustrates 7-alpha hydroxylase mRNA levels in liver in response to injections of LUVs, SUVs, or saline;
FIG. 9 illustrates key points about LUVs and atherosclerosis;
FIG. 10 illustrates plasma LDL unesterified cholesterol concentrations in response to injections of LUVs, SUVs or saline over time.
FIG. 11 illustrates plasma LDL esterified cholesterol concentrations in response to injections of LUVs, SUVs or saline over time;
FIG. 12 illustrates LDL esterified cholesterol concentrations in response to injections of LUVs, SUVs or saline;
FIG. 13 illustrates plasma VLDL esterified cholesterol concentrations in response to injections of LUVs, SUVs or saline;
FIGS. 14 and 15 illustrate HDL esterified cholesterol concentrations in response to injections of LUVs, SUVs or saline;
FIG. 16 illustrates the time course of cholesterol mobilization following an LUV injection into control or apoE KO mice;
FIG. 17 illustrates the time course of LUV clearance in control mice and apoE mice;
FIG. 18 illustrates that the compositions and methods of the present invention are effective in humans;
FIG. 19 illustrates a perspective view of an improved hemodialysis system of the present invention and improved method of hemodialysis;
FIG. 20 illustrates a perspective view of an improved peritoneal dialysis system 2000 and method of peritoneal dialysis;
FIG. 21 illustrates a perspective view of a variant of an improved peritoneal dialysis system with assaying means 2100 and method of peritoneal dialysis and analysis of spent fluid;
FIG. 22 illustrates a perspective view of an improved cardiac catheterization and/or angioplasty system 2200 and method of cardiac catheterization and/or angioplasty;.
FIG. 23 illustrates a perspective view of a variant of an improved cardiac catheterization and/or angioplasty system 2300 and method of cardiac catheterization and/or angioplasty;
FIG. 24 illustrates a graph of hepatic lipid contents in response to injections of LUVs, SUVs, or saline;
FIG. 25 illustrates plasma free cholesterol concentrations following repeated injections of SUVs or LUV (300 mg/kg) in NZW rabbits;
FIG. 26 illustrates plasma cholesterol ester concentrations following repeated injections of SUVs or LUV (300 mg/kg) in NZW rabbits;
FIG. 27 illustrates alternations in plasma components after repeated injections of SUVs; and,
FIG. 28 illustrates an agarose gel electrophoresis of whole plasma following repeated injections of LUVs, SUVs, or saline.

=> s l5 not l6

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  26 FILES SEARCHED...
L7           87 L5 NOT L6

=> s l7 and administ?
  20 FILES SEARCHED...
L8           19 L7 AND ADMINIST?

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DUPLICATE IS NOT AVAILABLE IN 'FEDRIP, ADISINSIGHT, PHAR'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L8
L9            19 DUP REM L8 (0 DUPLICATES REMOVED)
                 ANSWERS '1-4' FROM FILE WPIDS
                 ANSWERS '5-9' FROM FILE CAPLUS
                 ANSWERS '10-12' FROM FILE EMBASE
                 ANSWERS '13-15' FROM FILE USPAT2
                 ANSWER '16' FROM FILE BIOTECHDS
                 ANSWER '17' FROM FILE IFIPAT
                 ANSWER '18' FROM FILE ADISCTI
                 ANSWER '19' FROM FILE ADISINSIGHT

=> d bib abs 1-17

L9   ANSWER 1 OF 19  WPIDS (C) 2003 THOMSON DERWENT
AN   1995-030330 [04]   WPIDS
DNC  C1995-013640
TI   New dibenzofuran yl esters of N-heterocyclic carboxylic acids  - useful
     for reducing cholesterol uptake from intestinal tract.
DC   B02
IN   COMMONS, T J; STRIKE, D P
PA   (AMHP) AMERICAN HOME PROD CORP
CYC  1
PI   US 5373009    A  19941213 (199504)*       4p
ADT  US 5373009 A US 1994-190416 19940202
PRAI US 1994-190416   19940202
AN   1995-030330 [04]   WPIDS
AB   US   5373009 A UPAB: 19950201
     Dibenzofuran derivs. of formula (I) are new: R1, R2 = halogen, CF3, CN,
     NO2, 1-6C alkyl, 1-6C alkoxy, COOH, 2-7C alkanoyl, 2-7C alkanoyloxy, 2-7C
     alkoxycarbonyl, mono- or di(1-6C alkyl)aminocarbonyl or mono- or di(1-6C
     alkyl)aminocarbonyloxy; m,n and p = 0-2; R3 = 1-6C alkyl; X = O, S or
     CR4R5; R4, R5 = H or 1-6C alkyl, or CR4R5 = 3-8C carbocyclic ring. Also
     claimed is a method of reducing cholesterol uptake from the intestinal
     tract by admin. of (I).
          USE - (I) are cholesterol ester hydrolase
     (CEH) inhibitors for reducing cholesterol uptake from the intestinal
     tract. They may be used to treat e.g. atherosclerosis,
     familial hypercholesterolaemia, hyperlipaemia. (I) may be
     administered orally or parenterally
     Dwg.0/0

L9   ANSWER 2 OF 19  WPIDS (C) 2003 THOMSON DERWENT
AN   1991-361500 [49]   WPIDS
DNC  C1991-155829
TI   Decreasing absorption of fats and cholesterol through intestinal wall -
     comprises admin. of carbamate ester which acts as pancreatic
     cholesterol esterase inhibitor.
DC   B05
IN   QUINN, D M
PA   (UNIP) UNIV IOWA
CYC  1
PI   US 5066674    A  19911119 (199149)*
ADT  US 5066674 A US 1990-533079 19900604
PRAI US 1990-533079   19900604
AN   1991-361500 [49]   WPIDS
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AB US 5066674 A UPAB: 19930928
The carbamate ester is of formula Z-X-C(=Y)NHR (I), Z = 2-naphthyl (opt. substd. by 1-8C alkyl, halogen, or 1-8C alkoxy) or p-acetamidophenyl. X and Y = O. R = 1-8C alkyl.

USE/ADVANTAGE - (I) act as pancreatic **cholesterol esterase** (CEase) inhibitors, for use as hypolipadaemic and hypocaloric agents. They pass through the GI tract unchanged, as they are poorly absorbed into the blood-stream and are resistant to CEase-catalysed hydrolysis. The method is useful in the **treatment** of obesity and **atherosclerosis**. Unit dosage of (I) is 0.01-1.0 mg/kg. **administered** orally.

In an example, cpds. (I) tested as inhibitors of the CEase-catalysed hydrolysis of p-nitrophenyl butyrate. The half-life of irreversible inhibition in the presence of 10 power -5 M inhibitor was 0.86 minutes for 2-naphthyl-n-octyl carbamate, 2.3 minutes for p-acetamidophenyl-n-hexyl carbamate and 29 minutes for p-acetamidophenyl n-butyl carbamate.
0/0

L9 ANSWER 3 OF 19 WPIDS (C) 2003 THOMSON DERWENT
AN 1990-348258 [46] WPIDS
CR 1991-178095 [24]; 1996-087083 [09]
DNC C1990-151144
TI Inhibition of intestinal cholesterol absorption - by oral **admin** of non-absorbable inhibitor of cholesterol esterase, esp. high mol.wt. sulphated polysaccharide.
DC B04 D16
IN LANGE, L G; SPILBURG, C A
PA (LANG-I) LANGE L G; (SPIL-I) SPILBURG C A; (SCHI-I) SCHIERANO P
CYC 17
PI WO 9012579 A 19901101 (199046)* 49p
RW: AT BE CH DE DK ES FR GB IT LU NL SE
W: AU CA JP US
AU 9055356 A 19901116 (199107)
US 5017565 A 19910521 (199123) 8p
US 5063210 A 19911105 (199147) 11p
EP 469079 A 19920205 (199206)
R: AT BE CH DE ES FR GB IT LI LU NL SE
JP 04503813 W 19920709 (199234) 19p
AU 633569 B 19930204 (199312)
EP 469079 B1 19941207 (199502) EN 29p
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
DE 69014870 E 19950119 (199508)
ES 2064736 T3 19950201 (199511)
JP 08019001 B2 19960228 (199613) 19p
US 5616570 A 19970401 (199719)# 20p
CA 2053258 C 19980210 (199817)
US 5792832 A 19980811 (199839)
ADT US 5017565 A US 1989-340868 19890420; US 5063210 A US 1989-429398 19891031; EP 469079 A EP 1990-907923 19900420; JP 04503813 W JP 1990-506819 19900420, WO 1990-US2079 19900420; AU 633569 B AU 1990-55356 19900420; EP 469079 B1 EP 1990-907923 19900420, WO 1990-US2079 19900420; DE 69014870 E DE 1990-614870 19900420, EP 1990-907923 19900420, WO 1990-US2079 19900420; ES 2064736 T3 EP 1990-907923 19900420; JP 08019001 B2 JP 1990-506819 19900420, WO 1990-US2079 19900420; US 5616570 A Cont of WO 1990-US2079 19900420, Cont of US 1991-773875 19911018, US 1994-283723 19940801; CA 2053258 C CA 1990-2053258 19900420; US 5792832 A Cont of US 1989-429398 19891031, Cont of US 1989-434899 19891113, Cont of US 1992-856910 19920512, Div ex US 1994-350801 19941207, US 1995-461881 19950605
FDT JP 04503813 W Based on WO 9012579; AU 633569 B Previous Publ. AU 9055356, Based on WO 9012579; EP 469079 B1 Based on WO 9012579; DE 69014870 E Based on EP 469079, Based on WO 9012579; ES 2064736 T3 Based on EP 469079; JP 08019001 B2 Based on JP 04503813, Based on WO 9012579; US 5792832 A Cont of US 5173408
PRAI US 1989-429398 19891031; US 1989-340868 19890420; US 1994-283723

19940801; US 1989-434899 19891113; US 1992-856910 19920512; US 1994-350801 19941207; US 1995-461881 19950605

AN 1990-348258 [46] WPIDS

CR 1991-178095 [24]; 1996-087083 [09]

AB WO 9012579 A UPAB: 19991221

Ingestible food prod. contains an effective amt. of a non-absorbable synthetic cholesterol esterase inhibitor (I). Inhibiting the intestinal absorption of cholesterol comprises **admin**. p.o. a non-absorbable inhibitor of cholesterol esterase or an antibody directed against cholesterol esterase.

Reducing serum cholesterol levels comprises **admin**. of a synthetic non-absorbable sulphated polysaccharide in combination with an absorbed cholesterol synthesis blocker, triglyceride lipase inhibitor or fatty acyl cholesterol O-acyl transferase (ACAT) inhibitor.

USE/ADVANTAGE - (I), esp. sulphonated polysaccharides, decrease intestinal absorption of cholesterol and fatty acid by inhibiting pancreatic cholesterol esterase, which is a key enzyme involved in dietary cholesterol absorption. (I) are stable and can be incorporated in food prods., including baked prods. for dietary control of serum cholesterol levels and atherosclerosis (I) are potent inhibitors; are non-absorbable, so that side-effects are reduced; and are inexpensive. Doses of cholesterol synthesis blockers or ACAT inhibitors can be reduced, and side-effects minimized, by use with (I).

Dwg.0/10

ABEQ US 5017565 A UPAB: 19930928

Method of inhibiting human pancreatic **cholesterol esterase** in the alimentary tract comprises oral **admin**. of a 3-sulphated polysaccharide (I). (I) is pref. 3-sulphated alginic acid, pectin, amylopectin, chitin, dextran, cellulose agar or chitosan which are all soluble, potent inhibitors of human pancreatic **cholesterol esterase**.

USE - In inhibiting or decreasing cholesterol and fatty acid absorption.

In an example, Na alginate (150 mg) was **treated** with 5 cc glacial acetic acid for 2 hrs. at room temp., filtered and resuspended in 5 ml N,N-dimethylformamide. To stirred soln. 1.5 g SO3-pyridine complex was added over 30 mins. at room temp. and resulting mixt. stirred overnight for 16 hrs. 5 ml dry pyridine was then added and the sulphated alginic acid was pptd. with 10 ml acetone-MeOH (9:1) mixt. before dissolving in 50 ml H2O and adding IN NaOH to adjust pH to 8. Repptn. with 200 ml acetone-MeOH (9:1) mixt. produced the Na salt of sulphonated alginic acid. Cpd. was tested for **cholesterol esterase** inhibition and it had IC50 of 0.25 microg/ml or 1.0nM.

ABEQ US 5063210 A UPAB: 19930928

Inhibiting pancreatic **cholesterol esterase** comprises contacting it with a 3-sulphate polysaccharide of M.W. 10+ kDa (100+ kDa, 500+ kDa). Pref. the 3-sulphated polysaccharide is 3-sulphated alginic acid, pectin, amylopectin, chitin, dextran, cellulose, agar or chitosan (Fig.2). Prepn. is e.g. by **treating** chitosan with glacial HOAc, dissoln.e in DMFA and sulphation with SO3/pyridine.

USE - The method reduces the absorption of cholesterol and triglycerides from the intestine and their concns. in the blood stream so reducing risk of **atherosclerosis**, etc. The material can be eaten in a baked biscuit.

ABEQ EP 469079 B UPAB: 19950117

Use of a non-absorbable inhibitor of **cholesterol esterase** in the manufacture of an ingestible pharmaceutical compostion for inhibiting the intestinal absorption of cholesterol wherein said inhibitor is a 3-sulphated polysaccharide or an antibody to **cholesterol esterase**.

Dwg.0/7

ABEQ US 5616570 A UPAB: 19970512

A method for inhibiting the intestinal absorption of cholesterol in a mammal by **administering** orally a non-absorbable inhibitor of **cholesterol esterase** comprising a 3-sulphated

polysaccharide having a molecular weight greater than 100,000 Da.
Dwg.0/7

L9 ANSWER 4 OF 19 WPIDS (C) 2003 THOMSON DERWENT
AN 1989-292337 [40] WPIDS
DNC C1989-129545
TI Inhibition of intestinal cholesterol and fatty acid absorption - by **admin**. of heparin, its sub-fraction or heparinase.
DC B04 D16
IN KINNUNEN, P M; LANGE, L G; SPILBURG, C A
PA (LANG-I) LANGE L G; (CVTH-N) CV THERAPEUTICS; (JEWI-N) JEWISH HOSPITAL ST
CYC 13
PI WO 8908456 A 19890921 (198940)* 35p
RW: AT BE CH DE FR GB IT LU NL SE
W: AU JP
AU 8934348 A 19891005 (199001)
US 5352601 A 19941004 (199439) 14p
US 5429937 A 19950704 (199532) 13p
US 5492822 A 19960220 (199613) 12p
ADT WO 8908456 A WO 1989-US787 19890227; US 5352601 A CIP of US 1988-168424 19880315, Cont of US 1989-312255 19890222, Cont of US 1990-544212 19900626, Cont of US 1991-655289 19910214, US 1992-936103 19920826; US 5429937 A CIP of US 1988-168424 19880315, Cont of US 1989-312255 19890222, Cont of US 1990-544212 19900626, Cont of US 1991-655289 19910214, Div ex US 1992-936103 19920826, US 1994-311862 19940926; US 5492822 A CIP of US 1988-168424 19880315, Cont of US 1989-312255 19890222, Cont of US 1990-544212 19900626, Cont of US 1991-655289 19910214, Div ex US 1992-936103 19920826, Div ex US 1994-311862 19940926, US 1995-386433 19950210
FDT US 5429937 A Div ex US 5352601; US 5492822 A Div ex US 5352601, Div ex US 5429937
PRAI US 1989-312255 19890222; US 1988-168424 19880315; US 1990-544212 19900626; US 1991-655289 19910214; US 1992-936103 19920826; US 1994-311862 19940926; US 1995-386433 19950210
AN 1989-292337 [40] WPIDS
AB WO 8908456 A UPAB: 19930923
Inhibiting intestinal cell endogenous heparin mediated absorption of cholesterol or fatty acids in mammals comprises orally **administering** heparin, an active heparin subfraction or heparinase.

USE - Heparin can compete for binding to cholesterol esterase, displacing the enzyme from the membrane of the intestinal cell and greatly diminishing the intestinal absorption of cholesterol and cholesterol derived fatty acids. Also exogenous heparin displaces the pancreatic enzymes, such as triglyceride lipase which hydrolyse triglycerides into free fatty acids, from the membrane of the intestinal cell.
6
ABEQ US 5352601 A UPAB: 19941122
Recovery of purified human pancreatic **cholesterol esterase** fraction (Mr 52,000) comprises passing a soln. of the crude esterase (pH about 8.2) over or through 2-(diethylamino)ethyl-cellulose, when other esterases are bonded to the solid phase; and collecting the eluate contg. the required fraction. Opt. further purification is possible by binding impurities on hydroxyapatite and heparin-Sepharose adsorbents.

USE/ADVANTAGE - The enzyme catalyses the cleavage of cholesterol esters in the presence of heparin, heparinase or their active fragments, inhibiting the absorption of cholesterol or fatty acids in intestinal cells. The oral **administration** of heparin or heparinase provides prophylaxis and **therapy** for **atherosclerosis**.
Dwg.0/0
ABEQ US 5429937 A UPAB: 19950818
Soln. of purified human pancreatic **cholesterol esterase** of mol.wt. 100000 is prepd. from a dialysed soln. contg. protein impurities and similar **cholesterol esterase** protein of

various mol.wt. Process comprises (a) chromatographing the soln. obtd. on heparin agarose; (b) washing the impurities away; and (c) eluting and collecting the band contg. prod. of mol.wt. 100000.

USE - Used for inhibiting intestinal cholesterol absorption in mammals, and in the **treatment** of **atherosclerosis**.

Dwg.0/6

ABEQ US 5492822 A UPAB: 19960329

A method for recovering a solution of purified human pancreatic **cholesterol esterase** having a molecular weight of about 100,000, daltons comprising the steps:

(a) preparing a solution of dialysed human pancreatic cytosol including at least two molecular weight fractions of human pancreatic **cholesterol esterase**, one of which is the 100,000 daltons molecular weight fraction of human **cholesterol esterase**;

(b) passing the solution of dialysed pancreatic cytosol over a hydroxyapatite column and eluting all molecular weight fractions of **cholesterol esterase** present as a single peak to give a first eluent;

(c) passing the first eluent over a gel filtration column and collecting the 100,000 molecular weight fraction of **cholesterol esterase** as a single peak to give a second eluent including the 100,000 dalton molecular weight fraction of **cholesterol esterase** and protein impurities;

(d) dialysing the second eluent;

(e) passing the dialysed second eluent over a chromatography column containing a chromatography material selected from the group consisting of heparin agarose and heparin-Sepharose: and

(f) washing the chromatography column of step (e) and collecting a third eluent containing the purified **cholesterol esterase** having a molecular weight of about 100,000 daltons.

Dwg.0/6

L9 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 2002:54282 CAPLUS

DN 136:288794

TI Long-term **administration** of the HMG-CoA reductase inhibitor lovastatin in two patients with cholesteryl ester storage disease

AU Rassoul, F.; Richter, V.; Lohse, P.; Naumann, A.; Purschwitz, K.; Keller, E.

CS Department of Clinical Chemistry and Pathobiochemistry, University Leipzig/Working Group Health Promotion and Prevention of, Leipzig, D-04103, Germany

SO International Journal of Clinical Pharmacology and Therapeutics (2001), 39(5), 199-204
CODEN: ICTHEK; ISSN: 0946-1965

PB Dustri-Verlag Dr. Karl Feistle

DT Journal

LA English

AB In order to suppress de novo cholesterol and VLDL biosynthesis, a long-term **therapy** trial with lovastatin, a competitive inhibitor of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase, was initiated in two patients with cholesteryl ester storage disease (CESD), and concns. of plasma lipids were monitored over a period of 9 yr. We studied two male patients with enzymically confirmed CESD in whom long-term lovastatin **therapy** (8 and 9 yr) was begun at the age of 7 and 19 yr. The diagnosis of CESD was confirmed by the measurement of human **lysosomal acid lipase** (hLAL) activity in cultured skin fibroblasts and leukocytes. Restriction fragment length polymorphism (RFLP) anal. revealed that both subjects are homozygotes for the common CESD splice site mutation. Levels of serum lipids and lipoproteins were measured yearly. During the first year, total serum cholesterol decreased from 317 to 201 mg/dL in Patient A and from 228 to 120 mg/dL in Patient B, due mainly to the redn. of low-d. lipoprotein (LDL) cholesterol from 262 to 151 mg/dL in Patient A and from 166 to 66

mg/dL in Patient B. Accordingly, the LDL cholesterol : high d. lipoprotein (HDL) cholesterol ratio was markedly reduced in both patients after one year of **therapy**. The **treatment** was continued and, after 9 yr of further medication, low total cholesterol and LDL cholesterol levels were still maintained. The study demonstrates that HMG-CoA reductase inhibitors are well tolerated drugs during long-term **treatment** of CESD patients and may help to prevent the development of premature **atherosclerosis**.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1998:778770 CAPLUS
DN 130:148461
TI Cholesterol-lowering effects of NTE-122, a novel acyl-CoA:cholesterol acyltransferase (ACAT) inhibitor, on cholesterol diet-fed rats and rabbits
AU Azuma, Yukimasa; Kawasaki, Takashi; Ikemoto, Kiyohitò; Obata, Keisuke; Ohno, Katsutoshi; Sajiki, Nobuko; Yamada, Toshihiro; Yamasaki, Masahiro; Nobuhara, Yoichi
CS Central Research Institute, Nissin Food Products Co., Ltd., Shiga, 525-0055, Japan
SO Japanese Journal of Pharmacology (1998), 78(3), 355-364
CODEN: JJPAAZ; ISSN: 0021-5198
PB Japanese Pharmacological Society
DT Journal
LA English
AB Pharmacol. characterization of NTE-122 (trans-1,4-bis[[1-cyclohexyl-3-(4-dimethylamino phenyl)ureido]methyl]cyclohexane), a novel acyl-CoA:cholesterol acyltransferase (ACAT) inhibitor, was performed with both in vitro and in vivo assay systems. NTE-122 inhibited microsomal ACAT activities of various tissues (liver of rabbit and rat, small intestine of rabbit and rat, and aorta of rabbit) and cultured cells (HepG2 and CaCo-2), with IC50 values from 1.2 to 9.6 nM. The inhibition mode of NTE-122 was competitive for HepG2 ACAT. NTE-122 had no effect on other lipid metabolizing enzymes, such as 3-hydroxy-3-methylglutaryl-CoA reductase, acyl-CoA synthetase, **cholesterol esterase**, lecithin:cholesterol acyltransferase, acyl-CoA:sn-glycerol-3-phosphate acyltransferase and cholesterol 7.alpha.-hydroxylase up to 10 .mu.M. When NTE-122 was **administered** to the cholesterol diet-fed rats, serum and liver cholesterol levels were markedly reduced with an ED50 of 0.12 and 0.44 mg/kg/day, resp. In the cholesterol diet-fed rabbits, NTE-122 significantly lowered plasma and liver cholesterol levels at more than 2 mg/kg/day. These results indicate that NTE-122 is a potent, selective and competitive inhibitor of ACAT, making it a worth while **therapeutic** agent for hypercholesterolemia and **atherosclerosis**.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1982:433656 CAPLUS
DN 97:33656
TI Sex differences in aortic cholesterol esterase activity in rats, and changes of the activity following castration and gonadal hormone treatment
AU Tomita, T.; Yonekura, I.; Umegaki, K.; Okada, T.; Hayashi, E.
CS Dep. Pharmacol., Shizuoka Coll. Pharm. Sci., Shizuoka, Japan
SO Atherosclerosis (Shannon, Ireland) (1982), 43(2-3), 405-15
CODEN: ATHSBL; ISSN: 0021-9150
DT Journal
LA English
AB Sex differences in aortic **cholesterol esterase** [9026-00-0] activity and changes in the activity following castration and gonadal hormone **treatment** were investigated in rats. Differences in the enzyme activity were apparent after 2.5 mo and became most significant after 6 mo. The activity in the aorta and the liver was higher in female rats. Prepubertal orchiectomy increased the aortic

activity, feminizing the type of metab., whereas postpubertal orchiectomy and both pre- and postpubertal ovariectomy induced no change in the activity. The **administration** of testosterone [58-22-0] to female rats decreased the aortic activity, masculinizing the type of metab. However, the **administration** of testosterone or of 17.beta.-estradiol to male rats had no effect. Apparently, there are clear sex differences in aortic **cholesterol esterase** activity, and prepubertal exposure to androgens plays a crit. role in the sexual differentiation in aortic and hepatic cholesterol ester metab. The **administration** of testosterone can temporarily masculinize the type of metab. These results may partly explain the sexual differences in susceptibility to **atherosclerosis**.

L9 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1982:215450 CAPLUS
DN 96:215450
TI Lipid metabolism in arteriosclerotic arterial wall of rats
AU Morisaki, Nobuhiro; Murano, Shunichi; Shinomiya, Masaki; Sasaki, Norihiro; Shirai, Kohji; Matsuoka, Nobuo; Mizobuchi, Masato; Akikusa, Bunshiro; Saito, Yasushi; Kumagai, Akira
CS Sch. Med., Chiba Univ., Chiba, Japan
SO Atherosclerosis (Shannon, Ireland) (1982), 43(1), 51-7
CODEN: ATHSBL; ISSN: 0021-9150
DT Journal
LA English
AB Arteriosclerotic lesions were formed in rat aorta by the **administration** of vitamin D2, a high-fat diet, and a thyroid suppressing agent. This **treatment** increased the serum total cholesterol level 12-fold above the control level. In the arteriosclerotic lesions, the activities of lysosomal enzymes, such as acid phosphatase and acid lipase, were higher than in controls, that of acid **cholesterol esterase** was decreased, those of microsomal lipid-synthesizing enzymes, such as acyl-CoA synthetase and cholesterol ester synthesizing activity, were increased and that of neutral **cholesterol esterase** was decreased. Apparently, lipid metab. in arteriosclerotic lesions was changed, resulting in the accumulation of cholesterol esters in the aorta. **Administration** of a high-fat diet and a thyroid suppressing agent also increased the serum cholesterol levels to 12-fold above the control level, but did not induce arteriosclerotic lesions. After this **treatment**, the activities of hydrolyzing enzymes in the aorta increased, but the activities of lipid synthesizing enzymes increased. Apparently, lipid metab. in the aorta in this condition changes to compensate for the large influx of serum lipids and to prevent **arteriosclerosis**. The roles of the serum lipid level, cell injury, and lipid metab. in the aorta in forming arteriosclerotic lesions are discussed on the basis of these results.

L9 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1981:118985 CAPLUS
DN 94:118985
TI Estrogen **administration** early in life and the development of atherosclerosis
AU Subbiah, M. T. R.; Yunker, R.
CS Med. Cent., Univ. Cincinnati, Cincinnati, OH, 45267, USA
SO Pharmacology (1981), 22(2), 128-34
CODEN: PHMGBN; ISSN: 0031-7012
DT Journal
LA English
AB The effect of high doses of estrogen early in life on aortic **atherosclerosis** and cholesteryl ester metab. was investigated in female **atherosclerosis**-susceptible pigeons. Long-term estrogen (0.25 mg/kg/day) **administration** increased the severity of aortic **atherosclerosis**. Following short-term **administration** of estrogens, the concn. of aortic cholesterol was higher in estrogen-

treated pigeons with a marked increase in cholesteryl esters. Detn. of activities of enzymes concerned with cholesteryl ester metab. in aorta indicated an increase in cholesteryl ester synthetase, while no difference was noted in the 3 **cholesteryl ester hydrolases** located in subcellular fractions of aorta.

L9 ANSWER 10 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2000425785 EMBASE
TI Shosaikoto as a potential antiatherosclerotic agent.
AU Inoue M.
CS Dr. M. Inoue, Dept. of Pharmacognosy, Faculty of Pharmaceutical Sciences, Nagoya City University, 3-1 Tanabe-dori, Mizuho-ku, Nagoya 467-8603, Japan
SO Drug News and Perspectives, (2000) 13/7 (407-412).
Refs: 34
ISSN: 0214-0934 CODEN: DNPEED
CY Spain
DT Journal; General Review
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
036 Health Policy, Economics and Management
037 Drug Literature Index
LA English
SL English
AB Shosaikoto, a Kampo medicine used clinically to **treat** patients with chronic hepatitis or cirrhosis in Japan, displays immunoregulatory effects, especially on macrophage functions. Oral **administration** of shosaikoto influences the synthesis of humoral factors such as the interleukins, nitric oxide and prostaglandins in macrophages. In addition, phagocytic activity is enhanced by **treatment** with shosaikoto, resulting in an antigen that is effectively presented to T lymphocytes to produce more antibodies. The role of macrophages in the pathogenesis of **atherosclerosis** is well recognized, although a **therapeutic** agent targeted at macrophages has not yet been developed. When shosaikoto was **administered** to atherosclerotic rabbits, it did not exhibit antihyperlipidemic effects but did reduce the formation of atherosclerotic lesions. In addition, **treatment** with shosaikoto suppressed intimal hyperplasia in apoE-deficient mice fed a cholesterolenriched diet for nine weeks. Biochemical studies demonstrated that the mechanism of the antiatherosclerotic effect was partly due to the increase of oxidized low-density lipoprotein (oxLDL) elimination by macrophages, resulting from stimulation of oxLDL uptake through scavenger receptors, activation of acyl-CoA:cholesterol acyltransferase and **neutral cholesteryl ester hydrolase**, and increase of cholesterol elimination by high-density lipoprotein. Furthermore, shosaikoto is able to reverse the depression of macrophage functions caused by hyperlipidemia. These results indicate the potential of this medicine as a new type of preventive or **therapeutic** agent for **atherosclerosis**. (C) 2000 Prous Science.

L9 ANSWER 11 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 86158857 EMBASE
DN 1986158857
TI Prostaglandins, prostacyclin, and thromboxane in cardiovascular diseases.
AU Chan P.S.; Cervoni P.
CS Department of Cardiovascular Biological Research, Medical Research Division, American Cyanamid Co., Lederle Laboratories, Pearl River, NY 10965, United States
SO Drug Development Research, (1986) 7/4 (341-359).
CODEN: DDREDK
CY United States
DT Journal
FS 037 Drug Literature Index
030 Pharmacology
018 Cardiovascular Diseases and Cardiovascular Surgery
LA English
AB Prostaglandins appear to play an important role in or to be found

therapeutically useful in various cardiovascular diseases, such as hypertension, arrhythmias, ventricular fibrillation, arterial thrombosis, myocardial ischemia, myocardial infarction, certain types of angina pectoris, **atherosclerosis**, circulatory shock, and peripheral arterial diseases, etc. Prostacyclin and prostaglandins E1, E2, and D2 are considered beneficial, while thromboxane A2 and prostaglandin F(2.alpha.) are considered harmful and their formations should be inhibited. Inhibition of the formation of the vasodepressor prostaglandins, such as prostacyclin and prostaglandin E2, in humans and animals leads to increase in arterial blood pressure and total peripheral resistance as well as to decrease the efficacy of most antihypertensive drugs, which suggests that these vasodepressor prostaglandins play an important role in hypertension. Most prostaglandins exert antiarrhythmic activity. Prostacyclin and thromboxane synthetase inhibitors are particularly effective in myocardial infarction/reperfusion-induced arrhythmias and ventricular fibrillation (sudden cardiac death) where the classical antiarrhythmic agents are not very effective. Prostacyclin and thromboxane synthetase inhibitors are effective in reducing myocardial infarct size, increasing coronary blood flow, and inhibiting arterial thrombosis. **Atherosclerosis** may result from decreases in prostacyclin formation in the blood vessel wall due to inhibition by the high concentration of lipid peroxides in the blood. Prostacyclin stimulates **cholesterol ester hydrolase**, the enzyme that converts cholesterol ester to free cholesterol for mobilization out of the cells. PGE2 inhibits acyl CoA cholesterol-O-acyltransferase (ACAT), the enzyme that catalyzes the reesterification of free cholesterol. Therefore, prostacyclin, PGE2, and their stable analogs may be useful for the presention and induction of regression of **atherosclerosis**. Prostacyclin, PGE1, and other stable prostaglandin analogs, such as iloprost and viprostol, have been reported to be beneficial for the **treatment** of peripheral arterial disease. It is very likely that new drugs that affect the prostaglandin systems will be introduced for the prevention and **treatment** of various cardiovascular diseases in the very near future.

L9 ANSWER 12 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 80231776 EMBASE
DN 1980231776
TI Effects of phthalazinol (EG 626) on arterial lipolytic enzyme activities in the rat.
AU Tomita T.; Yonekura I.; Shirasaki Y.; et al.
CS Lab. Pharmacol., Shizuoka Coll. Pharmaceut. Sci., Shizuoka 422, Japan
SO Paroi Arterielle, (1979) 5/4 (181-184).
CODEN: PARTD6
CY France
DT Journal
FS 037 Drug Literature Index
029 Clinical Biochemistry
018 Cardiovascular Diseases and Cardiovascular Surgery
003 Endocrinology
030 Pharmacology
LA English
SL French
AB Phthalazinol (EG 626), a thromboxane A2 antagonist and cyclic AMP phosphodiesterase inhibitor, has been shown to prevent the **atherosclerosis** induced in cholesterol-fed rabbits. In an attempt to clarify the antiatherosclerotic mechanism, the effects of this compound on the lipolytic enzyme activities (**cholesterol esterase** and lipoprotein lipase) of rat aorta were examined in vivo. **Administration** of EG 626 (100-200 mg/kg, per os, daily, 1-2 weeks) affected neither the aortic lysosomal **cholesterol esterase** nor the acid phosphatase activity, whereas the lipoprotein lipase activity was significantly decreased by the **treatment**. These results suggest that with an elevation in HDL-cholesterol, a decrease in lipoprotein lipase activity after ingestion

of EG 626 might contribute, at least to some extent, to the prevention of arterial lipid accumulation.

L9 ANSWER 13 OF 19 USPAT2
AN 2002:119912 USPAT2
TI Imidazo-isoquinolin-5-one derivatives, pyrimido-isoquinolin-6-one derivatives and imidazo-naphthyridin-5-one derivatives
IN Elokdah, Hassan M., Yardley, PA, United States
Sulkowski, Theodore S., Wayne, PA, United States
Chai, Sie-Yearl, Lawrenceville, NJ, United States
Babiak, John, Martinsville, NJ, United States
PA Wyeth, Madison, NJ, United States (U.S. corporation)
PI US 6448255 B2 20020910
AI US 2001-965957 20010928 (9)
PRAI US 2000-237304P 20001002 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Rao, Deepak R.
LREP Nagy, Michael R.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 551
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antiatherosclerotic compounds are provided which have the following structure: ##STR1##

wherein:

R is hydrogen, lower alkyl, alkenyl, alkynyl, aryl, heteroaryl, or aryl or heteroaryl substituted with one or more members of the group consisting of alkyl, hydroxy, alkoxy, perfluoroalkyl, perfluoroalkoxy, alkylthio, nitro, amino, mono or di-alkylamino, and halogen;

D is C--H, carbon bound to R.sub.5 or nitrogen;

R.sub.1, R.sub.2, R.sub.3, and R.sub.4 are each independently hydrogen, alkyl, or taken together form a ring;

R.sub.5 is one or more groups selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, hydroxy, alkoxy, perfluoroalkyl, perfluoroalkoxy, alkylthio, nitro, amino, mono or di-alkylamino, or halogen;

n is an integer of 0-3;

or pharmaceutically acceptable salts thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 14 OF 19 USPAT2
AN 2002:85730 USPAT2
TI Amino thioxomethyl amino oxyacetic acid derivatives
IN Elokdah, Hassan M., 1487 Merrick Rd., Yardley, PA, United States 19067
Sulkowski, Theodore S., 316 Rockland Rd., Wayne, PA, United States 19087
PI US 6472430 B2 20021029
AI US 2001-965898 20010928 (9)
PRAI US 2000-237466P 20001002 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Killos, Paul J.
LREP Nagy, Michael R.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)

LN.CNT 701
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antiatherosclerotic compounds are provided which have the following structure: ##STR1##

wherein

R is lower alkyl;

R.sub.1 is hydroxy, amino, or lower alkoxy,

R.sub.2 and R.sub.3 are each independently hydrogen, alkyl or aryl;

Ar is phenyl, indanyl, benzhydryl, or phenyl substituted with one or more member selected from the group consisting of halogen, lower alkyl, perfluoroalkyl, lower alkoxy, perfluoroalkylalkoxy, dialkylamino, and aryloxy; or pharmaceutically acceptable salts thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 15 OF 19 USPAT2
AN 2001:128864 USPAT2
TI Oxetanone derivatives
IN Mullins, John Jason Gentry, San Francisco, CA, United States
PA 2 Pro Chemical, Dover, DE, United States (U.S. corporation)
PI US 6342519 B2 20020129
AI US 2000-746345 20001221 (9)
RLI Continuation-in-part of Ser. No. US 2000-698307, filed on 27 Oct 2000 Continuation-in-part of Ser. No. US 2000-618328, filed on 18 Jul 2000, now abandoned Continuation-in-part of Ser. No. US 1999-431551, filed on 29 Oct 1999, now patented, Pat. No. US 6235305
PRAI US 1999-165960P 19991117 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Solola, T. A.
LREP Lev, Robert G.
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 2078
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to novel oxetanone derivative compounds and processes for producing such derivatives that are useful as lipase inhibitors. Further the invention relates to processes for producing salts and for producing pharmaceutical compositions compounds comprising at least one such oxetanone derivative or salt, as well as methods for using such compounds and compositions for inhibiting lipases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 16 OF 19 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 2001-15416 BIOTECHDS
TI Use of **lysosomal-acid-lipase** for **treating atherosclerosis** and related diseases; lenti virus, adeno virus or adeno-associated virus vector-mediated gene transfer and expression in mouse for **atherosclerosis**, Wolman disease or cholesteryl ester storage disease gene **therapy**
AU Grabowski G A; Du H
PA Child.Hosp.Res.Found.Cincinnati
LO Cincinnati, OH, USA.
PI WO 2001056596 9 Aug 2001
AI WO 2001-US3481 2 Feb 2001
PRAI US 2001-180362 2 Feb 2001; US 2000-180362 4 Feb 2000
DT Patent

LA English
OS WPI: 2001-476267 [51]
AN 2001-15416 BIOTECHDS
AB A method of providing biologically active lipid hydrolyzing protein (**lysosomal-acid-lipase** (LAL)) or their mixtures, to cells of a mammal deficient in biologically active lipid hydrolyzing protein is new and involves **administering** into cells a vector (preferably a lenti virus, adeno virus, adeno-associated virus or virus-like vectors) containing and expressing a DNA sequence encoding LAL and expressing the DNA sequences in the cells. The LAL degrades lipoprotein-associated lipids presented to the lysosome. Every third day for 30 days, LAL was **administered** as an i.v. bolus via tail vein of lal-/- mice. The mice received a regular chow diet and LAL dosing was begun at 2 mth of age. Doses of LAL were 1.48 U in 1 x phosphate-buffered saline with 2% human serum albumin and 10 mM of dithiothreitol. Triglycerides from the liver, spleen and small intestine were determined by chemical analyses and showed that triglyceride concentration in the **treated** group was 65% reduced compared to an untreated control group. The method is useful in gene **therapy** to **treat atherosclerosis**, Wolman disease or cholesteryl ester storage disease. (61pp)

L9 ANSWER 17 OF 19 IFIPAT COPYRIGHT 2003 IFI
AN 2338058 IFIPAT;IFIUDB;IFICDB
TI CHOLESTEROL ESTER HYDROLASE INHIBITORS; ANTICHOLESTEROL AGENTS OR ANTILIPEMIC AGENTS
INF Commons, Thomas J, Wayne
Mewshaw, Richard E, Norristown
Strike, Donald P, St Davids, PA
IN Commons Thomas J; Mewshaw Richard E; Strike Donald P
PAF American Home Products Corporation, New York, NY
PA American Home Products Corp (3096)
EXNAM Shah, Mukund J
EXNAM Grumbling, Matthew V
AG Jackson, Richard K
PI US 5190940 19930302 (CITED IN 002 LATER PATENTS)
AI US 1991-796500 19911122
XPD 14 Sep 2010
RLI US 1990-582687 19900914 DIVISION 5112859
FI US 5190940 19930302
US 5112859
DT UTILITY; EXPIRED
FS CHEMICAL
GRANTED
CLMN 6
AB The compounds of the formula:

D R A W I N G

in which R1 is hydrogen or alkyl; R2 is alkyl, cycloalkyl, cycloalkylalkyl, phenylalkyl or alkylphenylalkyl; or R1 and R2 taken together complete a heterocyclic moiety of the formula:

D R A W I N G

in which X is

D R A W I N G

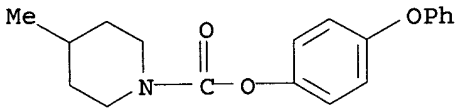
where R3,R4 and R5 are, independently hydrogen, alkyl, phenyl or substituted phenyl, in which the substituents are halogeno, alkoxy or trifluoromethyl; R6 is hydrogen, alkyl or gemdialkyl and n is one of the integers 0, 1 or 2, are **cholesterol ester hydrolase** inhibitors useful in the **treatment** of high serum cholesterol levels and associated disease states in the mammal such

as coronary heart disease, **atherosclerosis**, familial hypercholesterolemia, hyperlipemia, and the like.
CLMN 6

=> d 18-19

L9 ANSWER 18 OF 19 ADISCTI COPYRIGHT 2003 (ADIS)
AN 2001:8707 ADISCTI
DN 800867242
TI Long-term **administration** of the HMG-CoA reductase inhibitor lovastatin in two patients with cholesteryl ester storage disease.
ADIS TITLE: Lovastatin: therapeutic use.
Prevention of atherosclerosis
Long-term therapy in 2 patients with cholesterol ester storage disease: case report.
AU Rassoul F; Richter V; Lohse P; Naumann A; Purschwitz K; et al.
CS University Leipzig/Working Group Health Promotion and Prevention of Atherosclerosis (AGA) Leipzig, Leipzig, Germany.
SO International Journal of Clinical Pharmacology and Therapeutics (May 1, 2001), Vol. 39, pp. 199-204
DT Study
RE Hyperlipidaemia
FS Summary
LA English
WC 558

L9 ANSWER 19 OF 19 ADISINSIGHT COPYRIGHT 2003 (ADIS)
ACCESSION NUMBER: 1998:2847 ADISINSIGHT
SOURCE: Adis R&D Insight
DOCUMENT NO: 003268
CHANGE DATE: Jul 19, 2002
GENERIC NAME: WAY 121898
CHEMICAL NAME: 4-Phenoxyphenyl 4-methylpiperidin-1-yl carboxylate
MOLECULAR FORMULA: C18 H21 N O3
CAS REGISTRY NO.: 136100-14-6
STRUCTURE:



EPHMRA ATC CODE: C10A9 All other cholesterol/triglyceride reducers
WHO ATC CODE: C10A-X Other cholesterol and triglyceride reducers
HIGHEST DEV. PHASE: No Development Reported

COMPANY INFORMATION
ORIGINATOR: Wyeth (United States)
PARENT: Wyeth
OTHER: Pfizer Global Research and Development

WORD COUNT: 172

=> s l7 not l8
L10 68 L7 NOT L8

=> dup rem l10
DUPLICATE IS NOT AVAILABLE IN 'FEDRIP, ADISINSIGHT, PHAR'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L10

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L11          68 DUP REM L10 (0 DUPLICATES REMOVED)
                ANSWERS '1-21' FROM FILE WPIDS
                ANSWERS '22-38' FROM FILE CAPLUS
                ANSWERS '39-42' FROM FILE EMBASE
                ANSWERS '43-44' FROM FILE MEDLINE
                ANSWERS '45-48' FROM FILE DRUGU
                ANSWERS '49-50' FROM FILE USPAT2
                ANSWERS '51-54' FROM FILE FEDRIP
                ANSWER '55' FROM FILE PASCAL
                ANSWERS '56-57' FROM FILE BIOTECHDS
                ANSWERS '58-59' FROM FILE DRUGNL
                ANSWER '60' FROM FILE IFIPAT
                ANSWER '61' FROM FILE JICST-EPLUS
                ANSWER '62' FROM FILE ADISCTI
                ANSWERS '63-64' FROM FILE PHIN
                ANSWER '65' FROM FILE DRUGB
                ANSWER '66' FROM FILE FROSTI
                ANSWER '67' FROM FILE PHAR
                ANSWER '68' FROM FILE PROMT


=> d bib abs 1-44

L11  ANSWER 1 OF 68  WPIDS (C) 2003 THOMSON DERWENT
AN   2002-427098 [45]    WPIDS
DNN  N2002-335842        DNC C2002-121228
TI   Method for lipid assay by directly quantifying lipids particularly in
     blood component in presence of organosilicon compound, applicable in
     clinical examination e.g. diagnosis of arteriosclerosis and ischemic
     diseases.
DC   B04 D16 S03
IN   NAKAMURA, M; SAITO, K; YAMAMOTO, M; YAMAMOTO, S
PA   (DAUC) DAIICHI PURE CHEM CO LTD; (DAII-N) DAIICHI KAKAGU YAKUHIN KK
CYC  97
PI   WO 2002040707 A1 20020523 (200245)* JA   29p
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS KE KG KP KR KZ
            LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU
            SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
     AU 2002012760 A  20020527 (200261)
     JP 2002214239 A  20020731 (200265)       11p
ADT  WO 2002040707 A1 WO 2001-JP9899 20011113; AU 2002012760 A AU 2002-12760
     20011113; JP 2002214239 A JP 2001-347394 20011113
FDT  AU 2002012760 A Based on WO 200240707
PRAI JP 2000-346791   20001114
AN   2002-427098 [45]   WPIDS
AB   WO 200240707 A UPAB: 20020717
     NOVELTY - A method for lipid assay is by determining lipids in a blood
     component in the presence of an organosilicon compound.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
     following:
          (1) a reagent for lipid assay containing an organosilicon compound;
          (2) a reagent for assay HDL cholesterol containing an organosilicon
     compound, cholesterol esterase, cholesterol oxidase,
     peroxidase, and color-developing agent; and
          (3) a kit for assaying LDL cholesterol comprising a first reagent of
     an organosilicon compound, cholesterol esterase,
     cholesterol oxidase, peroxidase and one of the combination of any of the 2
     color-developing components; and a second reagent including the other
     combination of any 2 of the color-developing components, and a surfactant
     with low lipoprotein selectivity.
          USE - The method is lipid assay by directly quantifying lipids
     particularly in blood components, which is applicable in clinical
```

examination e.g. diagnosis of **arteriosclerosis** and ischemic diseases for prevention and **therapy**.

ADVANTAGE - Such direct method is convenient and accurate, without needing special equipment or conditions.

DESCRIPTION OF DRAWING(S) - Correlation between results by this method (see Example; 1B) as well as the control method (1A) and fractionation method in determining HDL cholesterol concentration in serum with a reagent containing an organosilicon compound. (Drawing includes non-English language text).

1A, 1B/3

L11 ANSWER 2 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 2003-203400 [20] WPIDS
DNC C2003-052047
TI New complexes of poly carbon chain anilide derivatives and cyclodextrins, useful for treatment of dyslipidemia, comprise water soluble Acyl Cholesterase Acyl Transferase inhibitors.
DC A96 B05
IN BOUGARET, J; GIL, A; IBARRA, M D; LEVERD, E; IBARRA, M
PA (FABR) FABRE MEDICAMENT SA PIERRE
CYC 27
PI FR 2823207 A1 20021011 (200320)* 27p
WO 2002083632 A1 20021024 (200320) FR
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU BR CA CN JP MX US ZA
ADT FR 2823207 A1 FR 2001-4855 20010410; WO 2002083632 A1 WO 2002-FR1224 20020409
PRAI FR 2001-4855 20010410
AN 2003-203400 [20] WPIDS
AB FR 2823207 A UPAB: 20030324
NOVELTY - Complexes (I), formed between Acyl **Cholesterase** Acyl Transferase (ACAT) - inhibiting anilide derivatives, comprise a poly carbon chain and cyclodextrins.

DETAILED DESCRIPTION - Complexes (I), formed between Acyl **Cholesterase** Acyl Transferase (ACAT) - inhibiting anilide derivatives, comprise a poly carbon chain, especially (S)-2'-3'-trimethyl-4'-hydroxy- alpha -dodecyl thio phenyl acetanilide (F12511) and cyclodextrins especially gamma -, beta -, and alpha -cyclodextrins or their hydroxypropyl, sulfobutyl ether or methylated derivatives.

INDEPENDENT CLAIMS are also included for:
(1) Production of (I); and
(2) Compositions (II) comprising (I).
the production of (I).
ACTIVITY - Antiarteriosclerotic; Antilipemic.
No biological data available.
MECHANISM OF ACTION - Acyl **Cholesterase** Acyl Transferase (ACAT) - inhibitors.
No biological data available.
USE - (I) are used for the **treatment** of dyslipidemia, e.g. hypercholesterolemia, or for the prevention of **atherosclerosis**.
ADVANTAGE - (I) provide improved solubility of the ACAT inhibitor in aqueous media.
DESCRIPTION OF DRAWING(S) - The figure shows thermo grams of the product and starting materials:
F12511 (RTM) a
Gamma cyclodextrin b
Mixture of F12511 (RTM) and gamma cyclodextrin c
Complex of F12511 (RTM) and gamma cyclodextrin d
(Drawing contains non-English language text).
Dwg.1/8

L11 ANSWER 3 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-091579 [10] WPIDS
DNC C2001-027035
TI Pretreatment of sample containing lipoproteins for quantifying cholesterol

e.g. when diagnosing and preventing arteriosclerosis and ischemic diseases, comprises treating the sample with an enzyme and optionally, a reaction accelerator.

DC B04 D16
IN MANABA, M; NAKAMURA, M; TANIGUCHI, Y; YAMAMOTO, M; MANABE, M
PA (DAUC) DAIICHI PURE CHEM CO LTD; (DAII-N) DAIICHI KAKAGU YAKUHIN KK
CYC 94
PI WO 2000078999 A1 20001228 (200110)* JA 38p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000054263 A 20010109 (200122)
JP 2001286297 A 20011016 (200176) 14p
BR 2000012311 A 20020319 (200228)
EP 1197564 A1 20020417 (200233) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CN 1357052 A 20020703 (200265)
KR 2002026446 A 20020410 (200267)
ADT WO 2000078999 A1 WO 2000-JP3860 20000614; AU 2000054263 A AU 2000-54263 20000614; JP 2001286297 A JP 2000-183053 20000619; BR 2000012311 A BR 2000-12311 20000614, WO 2000-JP3860 20000614; EP 1197564 A1 EP 2000-939057 20000614, WO 2000-JP3860 20000614; CN 1357052 A CN 2000-809286 20000614; KR 2002026446 A KR 2001-715534 20011203
FDT AU 2000054263 A Based on WO 200078999; BR 2000012311 A Based on WO 200078999; EP 1197564 A1 Based on WO 200078999
PRAI JP 2000-26737 20000203; JP 1999-174624 19990621
AN 2001-091579 [10] WPIDS
AB WO 200078999 A UPAB: 20010220

NOVELTY - A new pretreatment method for a sample containing lipoproteins, before measuring cholesterol contained in specific lipoproteins, comprises **treating** the sample with an enzyme and optionally, a reaction accelerator. The substrate for the enzyme is free cholesterol.

DETAILED DESCRIPTION - A new pretreatment method for quantifying cholesterol in a sample containing lipoproteins, before measuring cholesterol contained in specific lipoproteins, comprises **treating** the sample with an enzyme and optionally, a reaction accelerator. The substrate for the enzyme is free cholesterol.

The reaction accelerator is flufenamic acid, mefenamic acid, 2,2',6',2-terpyridine, tiglic acid, fusidic acid, betamethasone acetate, monensin or mevinolin.

INDEPENDENT CLAIMS are also included for the following:

(1) a method for quantifying cholesterol by measuring cholesterol in the specific lipoprotein after pretreatment with free cholesterol as substrate for the enzyme reaction, and optionally with a reaction accelerator added;

(2) a reagent for pretreating a sample for cholesterol quantitation comprising an enzyme with free cholesterol as substrate but without a substrate that can act on lipoproteins, or without **cholesterol esterase**, and optionally with the reaction accelerator;

(3) a kit for quantifying cholesterol comprising reagents including a first reagent of cholesterol oxidase and hydrogen peroxide-consuming material, and a second reagent of a substance for acting on the specific lipoproteins, **cholesterol esterase** and chromogenic reagent, or these ingredients together with cholesterol dehydrogenase, coenzyme and reaction accelerator in various combinations and orders of addition to effect reaction; and

(4) a reaction accelerator as defined above for enzymes like cholesterol oxidase or cholesterol dehydrogenase with free cholesterol as substrate.

USE - The method is useful for quantifying cholesterol e.g. with automatic analyzer for diagnosis and prevention of

arteriosclerosis and ischemic diseases.

ADVANTAGE - The method is convenient and can provide results with accuracy, efficiency and without resorting to polyanionic and precipitation techniques.

Dwg.0/3

L11 ANSWER 4 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1999-243579 [20] WPIDS
DNN N1999-181297 DNC C1999-070962
TI Reducing mammalian serum total cholesterol for treating hyperlipidemia, hypercholesterolemia and atherosclerosis.
DC B04 D13 D16 P14
IN CHERUKURI, R S V; CHERUVANKY, R; LYNCH, I E; MCPEAK, P; LYNCH, I; QURESHI, A A
PA (RICE-N) RICEX CO INC; (CHER-I) CHERUKURI R S V; (CHER-I) CHERUVANKY R; (LYNC-I) LYNCH I; (MCPE-I) MCPEAK P; (QURE-I) QURESHI A A; (RICE-N) RICEX CO
CYC 82
PI WO 9911144 A1 19990311 (199920)* EN 40p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9892098 A 19990322 (199931)
US 6126943 A 20001003 (200050)
US 6350473 B1 20020226 (200220)
US 2002086069 A1 20020704 (200247)
ADT WO 9911144 A1 WO 1998-US17881 19980828; AU 9892098 A AU 1998-92098 19980828; US 6126943 A Provisional US 1997-57870P 19970902, US 1998-143159 19980828; US 6350473 B1 Provisional US 1997-57870P 19970902, Cont of US 1998-143159 19980828, US 2000-624474 20000724; US 2002086069 A1 Provisional US 1997-57870P 19970902, Cont of US 1998-143159 19980828, Div ex US 2000-624474 20000724, US 2001-992332 20011116
FDT AU 9892098 A Based on WO 9911144; US 6350473 B1 Cont of US 6126943
PRAI US 1997-57870P 19970902; US 1998-143159 19980828; US 2000-624474 20000724; US 2001-992332 20011116
AN 1999-243579 [20] WPIDS
AB WO 9911144 A UPAB: 19990525

NOVELTY - Reducing mammalian serum total cholesterol, low density lipoprotein (LDL) cholesterol, apolipoprotein B and triglyceride levels, comprises ingesting a stabilized rice bran derivative obtained by enzyme **treatment** of rice bran, and/or an insolubilized fraction.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) preparing enzyme **treated** stabilized rice bran derivative comprising:

(a) mixing stabilized rice bran with an aqueous solution to form a 15-35% sold rice bran slurry;

(b) adding an enzyme to the slurry to convert starch to dextrin; and

(c) drying the slurry to obtain the stabilized rice bran derivative;

(2) the product of the preparation of (1); and

(3) a method for increasing the high density lipoprotein (HDL)/LDL cholesterol ratio in mammalian serum, comprising ingesting a stabilized rice bran derivative obtained by enzyme **treatment** of rice bran, and/or an insolubilized fraction.

ACTIVITY - Antiarteriosclerotic; Antilipemic.

MECHANISM OF ACTION - The major bioactive components present in the rice bran derivatives are tocopherols, tocotrienols, gamma -oryzanol, phytosterols, polyphenols, inositol, B vitamins, protein, fiber, and fat. The components act mostly synergistically, e.g. by enzyme inhibitions: three enzymes, namely 3-hydroxy-3-methylglutaryl-coenzyme A (HMGCoA) reductase, Acyl coenzyme A transferase (ACAT) and esterase are inhibited. HMGCoA reductase, a key enzyme involved in the cholesterol biosynthesis is inhibited by the tocotrienols, post transcriptionally, reducing the

synthesis of cholesterol resulting in low circulating cholesterol. Acyl coenzyme A transferase (ACAT), inhibition is brought about by:

(a) the prevention of cellular cholesterol esterification thereby enriching high density lipoprotein cholesterol (HDL) with free cholesterol;

(b) elevation of HDL, a positive effect, and decreased synthesis of very low density lipoprotein cholesterol (VLDL); and

(c) increased clearance of cholesterol as bile acids and bile salts.

The net result is lower circulating cholesterol. **Cholesterol esterases** are inhibited by cycloartenol, a component of -y-oryzanol, resulting in a slower hydrolysis of cholesterol esters and decreased absorption. This results in lower circulating total cholesterol. gamma -Oryzanol inhibits platelet aggregation, and aortic streaks thus reducing **atherosclerosis**. Rice bran derivatives contain a significant variety and concentration of antioxidants. Antioxidants such as tocopherols, tocotrienols, gamma -oryzanol, polyphenols as ferulic acid, and lipoic acid are involved in the repair of free radical damage, preventing low density lipoprotein cholesterol (LDL) oxidation, resulting in the reduction of vascular damage that can lead to cardiovascular disease. Cycloartenol, a component of gamma -oryzanol, has a structure similar to cholesterol and competes with receptor sites of cholesterol. This causes a sequestration of cholesterol as bile salts and bile pigments, thus maintaining lower levels of circulating cholesterol. Phytosterols and fiber facilitate cholesterol sequestration from the body through increased excretion of bile salts and bile acids, resulting in lower levels of circulating cholesterol. The protein, fat (with high levels of polyunsaturated and monounsaturated fatty acids), and B vitamins also contribute to the hypocholesterolemic effect.

USE - The method is used to **treat** subjects in which elevated levels of serum total cholesterol, LDL-cholesterol, VLDL-cholesterol, apolipoprotein B and triglyceride levels may lead to hyperlipidemia, cardiovascular disease, **atherosclerosis**, **arteriosclerosis** or xanthomatosis.

Dwg.0/0

L11 ANSWER 5 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1999-527033 [44] WPIDS
DNC C1999-154779
TI Preparation of 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester comprises carbonylation and coupling reaction, then carbonylation/hexylamine reaction, dealkylation and phenoxycarbonylation.
DC B03
IN JIRKOVSKY, I
PA (AMHP) AMERICAN HOME PROD CORP
CYC 1
PI US 5952506 A 19990914 (199944)* 7p
ADT US 5952506 A Provisional US 1997-44805P 19970424, US 1998-62515 19980417
PRAI US 1997-44805P 19970424; US 1998-62515 19980417
AN 1999-527033 [44] WPIDS
AB US 5952506 A UPAB: 19991026

NOVELTY - Preparation of 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester comprises reacting 1-benzyl- (or 1-methyl-) 4-hydroxypiperidine with carbonylating agent and 6-aminohexanol, followed by reaction with a carbonylating agent and hexylamine, followed by dealkylation and concomitant phenoxycarbonylation.

DETAILED DESCRIPTION - Preparation of 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester (I) comprises:

(a) reacting 1-benzyl-4-hydroxypiperidine or 1-methyl-4-hydroxypiperidine in an aprotic solvent at 0-70 deg. C (optionally in the presence of a tertiary amine) with:

(i) a carbonylating coupling reagent selected from carbonyldiimidazole, disuccinimidyl carbonate, 2,2'-carbonyl-bis(3,5-dioxo-1,2,4-oxazolidine) or 3,3'-carbonyl bis(5-phenyl-1,3-1,3,4-oxadiazole-

2(3H)thione) and;
(ii) 6-aminohexanol;
(b) reacting the resultant 4-((6-hydroxyhexyl)carbamoyloxy)piperidine derivative in an aprotic solvent at 0-70 deg. C (optionally in the presence of a tertiary amine) with:
(i) a carbonylating coupling reagent as above; and
(ii) hexylamine; and
(c) dealkylation and concomitant N-(4-phenoxy)phenoxycarbonylation of the intermediate 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)piperidine derivative with 4-phenoxyphenyl chloroformate in an aprotic solvent at 15-110 deg. C to give (I).
ACTIVITY - Antilipemic; antiarteriosclerotic.
MECHANISM OF ACTION - **Sterol-Esterase**-Inhibitor; Sterol-O-Acyltransferase-Inhibitor; ACAT-Inhibitor.
USE - For the large-scale preparation of (I) (claimed). (I) is useful for reducing cholesterol absorption and in the **treatment** of hypercholesterolemia, hyperlipidemia and **atherosclerosis**.
ADVANTAGE - (I) inhibits **cholesterol ester hydrolase** and acylcoenzyme A cholesterol acyltransferase. The preparation is carried out without isolation of intermediates and without changing solvents. The preparation gives improved purity, higher yields, lower costs, technical convenience and is less labor and time intensive than the prior art route in EP0635501-A1.
Dwg.0/0

L11 ANSWER 6 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1999-443009 [37] WPIDS
CR 1996-497796 [49]; 1999-069709 [06]; 1999-383976 [32]
DNC C1999-130466
TI Measuring the amount of cholesterol in low density lipoproteins to identify individuals at risk of arteriosclerosis and ischemic heart disease.
DC A96 B01 B04 D16
IN FUTATSUGI, M; HANADA, T; IMAJO, N; KOYAMA, I; MIKI, Y
PA (WAKP) WAKO PURE CHEM IND LTD; (WAKP) WAKO JUNYAKU KOGYO KK
CYC 29
PI US 5925534 A 19990720 (199937)* 28p
EP 964249 A2 19991215 (200003) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CA 2245261 A1 19991208 (200021) EN
JP 2000060600 A 20000229 (200022) 18p
KR 2000004844 A 20000125 (200061)
ADT US 5925534 A US 1998-128930 19980805; EP 964249 A2 EP 1998-306312 19980806; CA 2245261 A1 CA 1998-2245261 19980807; JP 2000060600 A JP 1999-67854 19990315; KR 2000004844 A KR 1998-32739 19980812
PRAI JP 1998-175396 19980608
AN 1999-443009 [37] WPIDS
CR 1996-497796 [49]; 1999-069709 [06]; 1999-383976 [32]
AB US 5925534 A UPAB: 19990914
NOVELTY - A method (X) for measuring the amount of cholesterol in low density lipoproteins (LDLs) in a sample, is new. (X) comprises:
(i) contacting the sample with at least 1 solution to carry out the reaction in the presence of a polyanion and an amphoteric surfactant; and
(ii) subjecting the reaction product obtained to an optical measurement to determine the amount of cholesterol.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(i) a reagent (A) for measuring the amount of cholesterol in LDLs, which comprises:
(1) **cholesterol esterase** (1) and cholesterol oxidase (2) or cholesterol dehydrogenase (3);
(2) a polyanion; and
(3) an amphoteric surfactant;
(ii) a reagent (B) for measuring the amount of cholesterol in LDLs,

which comprises:
(1) a polyanion;
(2) an amphoteric surfactant;
(3) (1);
(4) (2), peroxidase (4) and an oxidisable color producing reagent or
(3) and (5); and
(5) an aqueous medium;
(iii) a kit (I) for measuring the amount of cholesterol in LDLs,
which comprises:
(1) a reagent container (Ia) containing:
(a) a polyanion;
(b) an amphoteric surfactant;
(c) (1);
(d) (2), (4) and an oxidisable color producing reagent or (3) and
nicotinamide adenine dinucleotide (phosphate) (5); and
(e) an aqueous medium; and
(2) a reagent container (Ib) containing an aqueous medium;
(iv) a kit (II) for measuring the amount of cholesterol in LDLs,
which comprises:
(1) a reagent container (IIa) containing:
(a) a polyanion;
(b) an amphoteric surfactant;
(c) (1);
(d) (2);
(e) (4);
(f) an aqueous medium; and
(g) either a coupler or developer agent; and
(2) a reagent container (IIb) containing:
(a) an aqueous medium; and
(b) either a coupler or developer agent (depending on which chemical
is absent from (IIa);
(v) a kit (III) for measuring the amount of cholesterol in LDLs,
which comprises:
(1) a reagent container (IIIa) containing:
(a) a polyanion;
(b) an amphoteric surfactant;
(c) (1);
(d) (2);
(e) catalase (6);
(f) an aqueous medium; and
(g) either a coupler, developer agent and/or peroxidase; and
(2) a reagent container (IIIb) containing:
(a) a catalase inhibitor (7);
(b) an aqueous medium; and
(c) either a coupler, developer agent and/or peroxidase (depending on
which chemical is absent from (IIIa);
(vi) a kit (IV) for measuring the amount of cholesterol in LDLs,
which comprises:
(1) a reagent container (IVa) containing:
(a) a polyanion;
(b) an amphoteric surfactant;
(c) (1);
(d) (3);
(e) (5); and
(f) an aqueous medium; and
(2) a reagent container (IVb) containing:
(a) an aqueous medium;
(b) (2);
(c) (4);
(d) an oxidizable color producing reagent; and
(e) a cholesterol dehydrogenase inhibitor (8); and
(vii) a kit (V) for measuring the amount of cholesterol in LDLs,
which comprises:
(1) a reagent container (Va) containing:
(a) a polyanion;

(b) an amphoteric surfactant;
(c) (1);
(d) (2);
(e) (4);
(f) either a coupler and/or a developer; and
(g) an aqueous medium; and
(2) a reagent container (Vb) containing:
(a) an aqueous medium;
(b) (3);
(c) (5); and
(d) a cholesterol oxidase inhibitor (9).
USE - (X) may be used for measuring the amount of cholesterol in LDLs in samples from patients. LDL is a major carrier of cholesterol from the liver to other body tissues and increases in levels of LDLs appear to have an intimate relationship to the generation of arteriosclerosis and ischemic heart disease. Therefore, (I) may be used to measure LDL-cholesterol content, as an important indicator of diagnosis, therapy and prophylaxis of these diseases.
ADVANTAGE - (I) is a simple process with few stages and requiring few reagents (i.e. it does not require pretreatment of the sample to remove other non-LDL proteins (as compared to the ultra centrifugation and electrophoresis methods)) and may be carried out using widely available automated analyzers. (I) may be used to detect LDL-cholesterol content even if the sample contains greater than 400 mg/dl of triglycerides (compared to the Friedewald method).
Dwg.0/13

L11 ANSWER 7 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1998-609956 [51] WPIDS
DNC C1998-182788
TI 4-Carbamoyloxy-piperidine-1-carboxylate ester derivative preparation - in 3 stages from 4-hydroxy-piperidine derivative via new intermediates, used as cholesterol absorption inhibitor.
DC B03 B05
IN JIRKOVSKY, I
PA (AMHP) AMERICAN HOME PROD CORP
CYC 79
PI WO 9847870 A1 19981029 (199851)* EN 14p
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9869469 A 19981113 (199913)
ZA 9803399 A 19991229 (200006) 16p
ADT WO 9847870 A1 WO 1998-US6513 19980331; AU 9869469 A AU 1998-69469 19980331; ZA 9803399 A ZA 1998-3399 19980422
FDT AU 9869469 A Based on WO 9847870
PRAI US 1997-845565 19970424
AN 1998-609956 [51] WPIDS
AB WO 9847870 A UPAB: 19981223
Preparation of 4-[(6-hexylcarbamoyloxy)- hexylcarbamoyl]piperidine-1-carboxylic acid 4-phenoxyphenyl ester (I) comprises: (a) reacting 1-(benzyl or methyl)-4-hydroxypiperidine (II) with a carbonylating coupling reagent and 6-aminohexanol (III) in an aprotic solvent at 0-70 deg. C, optionally in the presence of a tertiary amine; (b) reacting the resultant 1-(benzyl or methyl)-4-[(6-hydroxyhexyl)carbamoyloxy]-piperidine (IV) with hexylamine (V) under the conditions of step (1); and (c) dealkylation and concomitant N-(4-phenoxy)-phenoxycarbonylation of the intermediate 1-(benzyl or methyl)-4-[6-(hexylcarbamoyloxy)-hexylcarbamoyloxy]piperidine (VI) with 4-phenoxyphenyl chloroformate (VII) in an aprotic solvent 15-110 deg. C. Also claimed are novel intermediates (IV), (VI) and (VII). Step (c) is also claimed as a separate process.
USE - (I), described in EP 635501, inhibits both **cholesterol**

ester hydrolase and acyl-coenzyme A cholesterol acyltransferase, resulting in a reduction of cholesterol absorption. Possible uses include **treatment** of hypercholesterolaemia, hyperlipidaemia and **atherosclerosis**.

ADVANTAGE - This method utilises a single solvent throughout, requires no purification of intermediates and is suitable for large-scale production. The yield and purity of (I) are higher than in the normal laboratory-scale synthesis and the method is much less labour intensive. Dwg.0/0

L11 ANSWER 8 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1998-467731 [40] WPIDS
DNN N1998-364435 DNC C1998-141911
TI Determination of skin cholesterol levels - by enzymatic reaction in vessel sealed to skin surface.
DC B04 D16 S03
IN LOPUKHIN, J M; PARFENOV, A S; LOPUKHIN YU, M; LOPUKHIN, Y M
PA (PARF-I) PARFENOV A S; (IMII-N) IMI INT MEDICAL INNOVATIONS INC; (LOPU-I) LOPUKHIN YU M; (LOPU-I) LOPUKHIN J M
CYC 82
PI WO 9837424 A1 19980827 (199840)* RU 16p
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9857846 A 19980909 (199905)
EP 987553 A1 20000322 (200019) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
BR 9807594 A 20000222 (200024)
RU 2130189 C1 19990510 (200026)
JP 2001513883 W 20010904 (200165) 15p
US 6365363 B1 20020402 (200226)
ADT WO 9837424 A1 WO 1998-RU10 19980126; AU 9857846 A AU 1998-57846 19980126; EP 987553 A1 EP 1998-901608 19980126, WO 1998-RU10 19980126; BR 9807594 A BR 1998-7594 19980126, WO 1998-RU10 19980126; RU 2130189 C1 RU 1997-102570 19970220; JP 2001513883 W JP 1998-536529 19980126, WO 1998-RU10 19980126; US 6365363 B1 WO 1998-RU10 19980126, US 1999-367724 19991110
FDT AU 9857846 A Based on WO 9837424; EP 987553 A1 Based on WO 9837424; BR 9807594 A Based on WO 9837424; JP 2001513883 W Based on WO 9837424; US 6365363 B1 Based on WO 9837424
PRAI RU 1997-102570 19970220
AN 1998-467731 [40] WPIDS
AB WO 9837424 A UPAB: 19981008
Determination of skin cholesterol levels comprises sealing an open-bottomed vessel by its base to the skin surface; adding a buffer solution (pH 6.8) containing 2.0-2.5 U cholesterol oxidase, 0.04-0.06 wt.% sodium deoxycholate and 0.1-0.2 wt.% 3-(dodecyldimethyl ammonium)-propane sulphonate; determining the cholesterol concentration in the reaction mixture by measuring the hydrogen peroxide concentration, and calculating the cholesterol content of the skin from the determined cholesterol concentration.

The reaction mixture also contains 3-5 U **cholesterol esterase**. The hydrogen peroxide concentration is measured: (a) by spectrophotometry after adding a peroxidase and a [chromogenic] substrate; (b) by immersing an electrochemical sensor in the reaction mixture, or (c) by immersing a colorimetric indicator (strip) in the reaction mixture.

USE - The method is used for early diagnosis of **atherosclerosis** and for monitoring **atherosclerosis therapy**.

ADVANTAGE - The method is more specific, simpler, more broadly applicable and more accurate than prior art methods (cf. US 5489510). Dwg.3/3

L11 ANSWER 9 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1998-457043 [39] WPIDS
DNC C1998-138208
TI Selective **cholesterol esterase** transport protein (CETP) activity inhibitors - comprise new and known o-thio-aniline derivatives, useful for **treating arteriosclerosis** and hyperlipaemia.
DC B03 B05
IN MAEDA, K; OKAMOTO, H; SHINKAI, H; OKAMATO, H; SHINAKI, H
PA (NISB) JAPAN TOBACCO INC
CYC 82
PI WO 9835937 A1 19980820 (199839)* JA 158p
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS KE KG KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
ZA 9801119 A 19981125 (199901) 134p
AU 9857818 A 19980908 (199904)
JP 11049743 A 19990223 (199918) 83p
JP 2894445 B2 19990524 (199926) 77p
JP 11222428 A 19990817 (199943) 74p
NO 9903869 A 19990923 (199951)
CZ 9902788 A3 20000216 (200016)
BR 9807222 A 20000523 (200035)
CN 1252053 A 20000503 (200036)
EP 1020439 A1 20000719 (200036) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT RO SE
SK 9901095 A3 20000516 (200036)
AU 728979 B 20010125 (200111)
NZ 337122 A 20010223 (200115)
KR 2000070982 A 20001125 (200131)
MX 9907423 A1 20000701 (200134)
HU 2000002483 A2 20010528 (200140)
JP 3290962 B2 20020610 (200241) 75p
US 6426365 B1 20020730 (200254)
KR 324183 B 20020216 (200257)
RU 2188631 C2 20020910 (200276)
SK 282973 B6 20030109 (200309)
NO 314228 B1 20030217 (200318)
ADT WO 9835937 A1 WO 1998-JP542 19980210; ZA 9801119 A ZA 1998-1119 19980211; AU 9857818 A AU 1998-57818 19980210; JP 11049743 A JP 1998-26688 19980123; JP 2894445 B2 JP 1998-26688 19980123; JP 11222428 A Div ex JP 1998-26688 19980123, JP 1998-296593 19980123; NO 9903869 A WO 1998-JP542 19980210, NO 1999-3869 19990811; CZ 9902788 A3 WO 1998-JP542 19980210, CZ 1999-2788 19980210; BR 9807222 A BR 1998-7222 19980210, WO 1998-JP542 19980210; CN 1252053 A CN 1998-804042 19980210; EP 1020439 A1 EP 1998-901574 19980210, WO 1998-JP542 19980210; SK 9901095 A3 WO 1998-JP542 19980210, SK 1999-1095 19980210; AU 728979 B AU 1998-57818 19980210; NZ 337122 A NZ 1998-337122 19980210, WO 1998-JP542 19980210; KR 2000070982 A WO 1998-JP542 19980210, KR 1999-707248 19990811; MX 9907423 A1 MX 1999-7423 19990811; HU 2000002483 A2 WO 1998-JP542 19980210, HU 2000-2483 19980210; JP 3290962 B2 Div ex JP 1998-26688 19980123, JP 1998-296593 19980123; US 6426365 B1 WO 1998-JP542 19980210, US 1999-367299 19991223; KR 324183 B WO 1998-JP542 19980210, KR 1999-707248 19990811; RU 2188631 C2 WO 1998-JP542 19980210, RU 1999-119494 19980210; SK 282973 B6 WO 1998-JP542 19980210, SK 1999-1095 19980210; NO 314228 B1 WO 1998-JP542 19980210, NO 1999-3869 19990811
FDT AU 9857818 A Based on WO 9835937; JP 2894445 B2 Previous Publ. JP 11049743; CZ 9902788 A3 Based on WO 9835937; BR 9807222 A Based on WO 9835937; EP 1020439 A1 Based on WO 9835937; AU 728979 B Previous Publ. AU 9857818, Based on WO 9835937; NZ 337122 A Based on WO 9835937; KR 2000070982 A Based on WO 9835937; HU 2000002483 A2 Based on WO 9835937; JP 3290962 B2 Previous Publ. JP 11222428; US 6426365 B1 Based on WO 9835937; KR 324183 B Previous Publ. KR 2000070982, Based on WO 9835937; RU 2188631

C2 Based on WO 9835937; SK 282973 B6 Previous Publ. SK 9901095, Based on WO 9835937; NO 314228 B1 Previous Publ. NO 9903869

PRAI JP 1998-26688 19980123; JP 1997-44836 19970212; JP 1997-165085 19970605

AN 1998-457043 [39] WPIDS

AB WO 9835937 A UPAB: 19981001

Cholesterol esterase transport protein (CETP) activity inhibitors contain compounds of formula (I), their prodrugs, salts, hydrates or solvates. R = 1-10C alkyl, 2-10C alkenyl or halogenated 1-4C lower alkyl; 3-10C cycloalkyl, 5-8C cycloalkenyl, 3-10C cycloalkyl 1-10C alkyl, aryl or aralkyl (all optionally substituted), or 5- or 6-membered heterocycle with 1-3 N, O or S; X1-X4 = H, halo, 1-4C lower alkyl, optionally substituted by halo, 1-4C lower alkoxy, cyano, nitro, acyl or aryl; Y = CO or SO2; and Z = H or mercapto-protecting group. Also claimed are compounds of formula (Ia), their prodrugs, salts, hydrates or solvates. R' = 2-10C cycloalkyl or 5-8C cycloalkenyl (both optionally substituted); and Z1' = H or a group of formula (a').

USE - (I) are useful for preventing and/or **treating arteriosclerosis** and hyperlipaemia (claimed).

ADVANTAGE - (I) selectively inhibit CETP activity and thus increase high-density lipoproteins whilst reducing the **arteriosclerosis** -causing low-density lipoproteins.

Dwg.0/0

L11 ANSWER 10 OF 68 WPIDS (C) 2003 THOMSON DERWENT

AN 1996-433959 [43] WPIDS

CR 1996-454869 [45]

DNN N1996-365570 DNC C1996-136285

TI Quantitating cholesterol in low density lipoprotein for detecting arteriosclerosis - by removing high density lipoprotein, reacting with cholesterol ester hydrolase and oxidase and measuring e.g. hydrogen peroxide.

DC A89 B04 D16 S03

IN MIIKE, A; MIYAUCHI, K

PA (KYOW) KYOWA MEDEX KK; (KYOW) KYOWA MEDEX CO LTD

CYC 26

PI WO 9628734 A1 19960919 (199643)* JA 36p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA CN JP KR MX US
AU 9649553 A 19961002 (199703)
EP 763741 A1 19970319 (199716) EN 20p
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 08527481 X 19970624 (199735)
KR 97703531 A 19970703 (199829)
US 5807696 A 19980915 (199844)
AU 702443 B 19990218 (199919)
MX 9605627 A1 19980701 (200012)
CN 1148430 A 19970423 (200109)
JP 3256241 B2 20020212 (200213) 14p
KR 276749 B 20010601 (200223)
MX 204009 B 20010831 (200239)
TW 480338 A 20020321 (200308)

ADT WO 9628734 A1 WO 1996-JP664 19960315; AU 9649553 A AU 1996-49553 19960315; EP 763741 A1 EP 1996-906036 19960315, WO 1996-JP664 19960315; JP 08527481 X JP 1996-527481 19960315, WO 1996-JP664 19960315; KR 97703531 A WO 1996-JP664 19960315, KR 1996-706421 19961113; US 5807696 A WO 1996-JP664 19960315, US 1996-737504 19961113; AU 702443 B AU 1996-49553 19960315; MX 9605627 A1 MX 1996-5627 19961115; CN 1148430 A CN 1996-190186 19960315; JP 3256241 B2 JP 1996-527481 19960315, WO 1996-JP664 19960315; KR 276749 B WO 1996-JP664 19960315, KR 1996-706421 19961113; MX 204009 B MX 1996-5627 19961115; TW 480338 A TW 1996-111384 19960918

FDT AU 9649553 A Based on WO 9628734; EP 763741 A1 Based on WO 9628734; JP 08527481 X Based on WO 9628734; KR 97703531 A Based on WO 9628734; US 5807696 A Based on WO 9628734; AU 702443 B Previous Publ. AU 9649553, Based on WO 9628734; JP 3256241 B2 Based on WO 9628734; KR 276749 B

Previous Publ. KR 97703531, Based on WO 9628734
PRAI JP 1995-57307 19950316
AN 1996-433959 [43] WPIDS
CR 1996-454869 [45]
AB WO 9628734 A UPAB: 20030204
Quantitating cholesterol in a low density lipoprotein (LDL) comprises: (a) eliminating cholesterol in a high density lipoprotein (HDL) from an LDL-contg. sample; (b) **treating** the resulting sample with **cholesterol ester hydrolase** and a cholesterol oxidase or cholesterol oxidoreductase; and (c) measuring the amt. of hydrogen peroxide or reduced coenzyme.
USE - The process is useful in the detection of **arteriosclerosis**.
Dwg.1/3

L11 ANSWER 11 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1995-274903 [36] WPIDS
DNC C1995-124690
TI New heterocyclic oxime-carbamate derivs. - used as **cholesterol ester hydrolase** inhibitors for reducing blood cholesterol level, e.g. for **treating atherosclerosis**.
DC B05
IN FELMAN, S W; JIRKOVSKY, I; MEMOLI, K A
PA (AMHP) AMERICAN HOME PROD CORP
CYC 1
PI US 5438056 A 19950801 (199536)* 15p
ADT US 5438056 A US 1993-131820 19931005
PRAI US 1993-131820 19931005
AN 1995-274903 [36] WPIDS
AB US 5438056 A UPAB: 19950918
Heterocyclic oxime carbamates of formula (I) are new: R1, R2 = thienyl, naphthyl, phenyl (opt. substd. by halogen, OMe or di-(1-3C alkyl)-amino) or substd. furanonyl of formula (a): or CR1R2 = 5H-indeno (1,2-b)pyridin-5-ylidene, 9H-xanthen-9-ylidene or 10,10-dioxo-9H-thiaxanthen-9-ylidene; R3, R4 = H or 4-20C hydrocarbyl; or NR3R4 = 4-(R8)-piperidino; R5, R6 = 1-3C alkyl, 5-7C cycloalkyl or phenyl (opt. substd. by 1-5C alkyl or halogen); R7 = H or halogen; R8 = 1-3C alkyl.
USE - (I) inhibit **cholesterol ester hydrolase**, and are useful for lowering, blood cholesterol (claimed), and may be useful for **treating** e.g. **atherosclerosis**, familial hypercholesterolaemia and hyperlipaemia.
Dwg.0/0

L11 ANSWER 12 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1995-138961 [18] WPIDS
DNC C1995-064231
TI New di benzo-furanyl-alkyl-carbamate derivs. - are **cholesterol ester hydrolase** inhibitors for **treating atherosclerosis** etc..
DC B02
IN COMMONS, T J; MEWSHAW, R E; STRIKE, D P
PA (AMHP) AMERICAN HOME PROD CORP
CYC 1
PI US 5401769 A 19950328 (199518)* 5p
ADT US 5401769 A US 1994-190402 19940202
PRAI US 1994-190402 19940202
AN 1995-138961 [18] WPIDS
AB US 5401769 A UPAB: 19950518
Dibenzofuranyl-N-alkyl carbamate derivs. of formula (I) are new: R1, R2 = H, F, Cl, Br, I, CF3, CN, NO2, 1-6C alkyl, 1-6C alkoxy, CO2H, 2-7C alkylcarbonyl, 2-7C alkylcarbonyloxy, 2-7C alkoxycarbonyl, 2-7C alkoxycarbonyloxy, mono- or di(1-6C alkyl)aminocarbonyl or mono- or di(1-6C alkyl)aminocarbonyloxy; R3 = H or 1-6C alkyl; R4 = 2-18C alkyl, 3-8C cycloalkyl, 1-6C alkyl or 7-18C phenylalkyl (opt. ring substd. by 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN, CF3 or phenyl).

USE - (I) inhibit the absorption of cholesterol from the intestinal tract by inhibiting **cholesterol ester hydrolase** (CEH). They are therefore used to **treat atherosclerosis**, familial hypercholesterolaemia, and hyperlipidaemia.
Dwg.0/0

L11 ANSWER 13 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1995-053622 [08] WPIDS
DNC C1995-024413
TI New tris carbamic acid ester(s) are ACAT inhibitors - useful for treating e.g. atherosclerosis, familial hypercholesterolaemia and hyperlipaemia.
DC B03
IN COMMONS, T J; LACLAIR, C M; STRIKE, D P; COMMONS, T J W
PA (AMHP) AMERICAN HOME PROD CORP
CYC 29
PI EP 635501 A1 19950125 (199508)* EN 35p
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE
AU 9467520 A 19950202 (199513)
CA 2128116 A 19950122 (199516)
FI 9403441 A 19950122 (199516)
BR 9402852 A 19950404 (199520)
JP 07089934 A 19950404 (199522) 27p
NZ 264032 A 19951221 (199606)
ZA 9405214 A 19960327 (199619) 55p
HU 70942 T 19951128 (199733)
BR 1100752 A3 19980505 (199825)
SG 47596 A1 19980417 (199826)
IL 110302 A 19980615 (199836)
AU 692157 B 19980604 (199839)
HU 216790 B 19990830 (199940)
US 5952354 A 19990914 (199944)
RU 2130928 C1 19990527 (200027)
TW 369527 A 19990911 (200035)#
ADT EP 635501 A1 EP 1994-305305 19940719; AU 9467520 A AU 1994-67520 19940718; CA 2128116 A CA 1994-2128116 19940715; FI 9403441 A FI 1994-3441 19940720; BR 9402852 A BR 1994-2852 19940718; JP 07089934 A JP 1994-165075 19940718; NZ 264032 A NZ 1994-264032 19940718; ZA 9405214 A ZA 1994-5214 19940715; HU 70942 T HU 1994-2108 19940715; BR 1100752 A3 BR 1997-1100752 19970512; SG 47596 A1 SG 1996-3025 19940718; IL 110302 A IL 1994-110302 19940713; AU 692157 B AU 1994-67520 19940718; HU 216790 B HU 1994-2108 19940715; US 5952354 A US 1993-95140 19930721; RU 2130928 C1 RU 1994-26296 19940715; TW 369527 A TW 1994-100154 19940110
FDT AU 692157 B Previous Publ. AU 9467520; HU 216790 B Previous Publ. HU 70942
PRAI US 1993-95140 19930721; TW 1994-100154 19940110
AN 1995-053622 [08] WPIDS
AB EP 635501 A UPAB: 19950602
Tris carbamic acid esters of 4 - 8 membered azacycloalkanols of formula (I) and their salts are new; p = 0 - 4, Z = -Ar1, -Ar1-Ar2-, -Ar1-O-Ar2, -Ar1-S-Ar2, -Ar1-O-C(O)-Ar2, -Ar1-C(O)-O-Ar2, -Ar1-C(O)-Ar2, -Ar1-(CH2)1-20-Ar2, -Ar1-(CH2)1-20-O-Ar2, -Ar1-O-(CH2)1-20-Ar2, -Ar1-(CR6=CR6)1-3-Ar2, -(CR6=CR6)1-3-Ar2 or -Ar1-NR7-Ar2; R6 = H or 1-8C alkyl; R7 = H, 1-8C alkyl, 1-8C alkylcarbonyl or 1-8C alkoxycarbonyl; Ar1, Ar2 = Ph, naphthyl, furanyl, benzofuranyl, pyrazinyl, thienyl, benzothienyl, imidazolyl, benzoxazolyl, thiazolyl, benzthiazolyl, indenyl, indolyl, quinolinyl, benzotriazolyl, carbazolyl, benzimidazolyl or fluorenyl etc. (all opt. substd.); A = a bridging gp. selected from 1-20C hydrocarbyl opt. unsatd. with 1-6 sites of olefinic and/or acetylenic unsaturation, -(CH2)m-W-(CH2)n- or -(CH2)b-Y-(CH2)c-; m, n = 1 - 19; m + n = 2 - 20; W = -O-, -S- or NR14; R14 = H, 1-20C alkyl, 1-20C alkylcarbonyl, 1-20C alkoxycarbonyl or benzyl; b, c = 0 - 20; b + c = 1 - 20, Y = phenylene, pyridinylene, naphthylene, pyrrolylene or a gp. of formula (ii) - (v) etc.; R15 = H, 1-8C alkyl, 1-20C alkylcarbonyl, 1-20C alkoxycarbonyl or benzyl; R1, R2 = H, 1-8C alkyl, 1-8C alkoxy, 1-8C alkylcarbonyl, OH, CN, 1-8C alkylcarbonyloxy or -(CH2)0-6-NR18R19; R18 =

1-8C alkyl, 1-8C alkoxycarbonyl or 1-8C alkylcarbonyl; R19 = H or 1-8C alkyl; R3 = H, 1-8C alkyl or 7-15C arylalkyl; aryl = Ph opt. substd. by 1-6C alkyl; R4, R5 = H, 1-20C alkyl, 2-20C alkenyl, 3-10C cycloalkyl, -(CH2)1-20-(3-10C cycloalkyl), -(CH2)1-20-Ar1 or -(CH2)1-20NR20R21; R20 = 1-20C alkyl, 2-20C alkenyl, 1-20C alkylcarbonyl, 1-20C alkoxycarbonyl or benzyl; R21 = H or 1-20C alkyl;

USE - (I) inhibit absorption of cholesterol from the intestinal tract and inhibit enzymes **cholesterol ester hydrolase** (CEH) and acyl-CoA cholesterol acyltransferase (ACAT). (I) are useful for **treating atherosclerosis**, familial hypercholesterolaemia and hyperlipidaemia.

Dwg.0/0

L11 ANSWER 14 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1994-191540 [23] WPIDS
CR 1992-415936 [50]
DNN N1994-150710 DNC C1994-087622
TI Assay or isolation of lipoprotein (a) - using a lectin attached to a solid support to specifically bind lipoprotein (a) in a liq. sample.
DC B04 D16 S03
IN SEMAN, L J
PA (SEMA-I) SEMAN L J
CYC 1
PI US 5320968 A 19940614 (199423)* 7p
ADT US 5320968 A CIP of US 1991-704457 19910523, US 1993-21189 19930223
PRAI US 1991-704457 19910523; US 1993-21189 19930223
AN 1994-191540 [23] WPIDS
CR 1992-415936 [50]
AB US 5320968 A UPAB: 19940727
Assaying for lipoprotein (a) in a liq. sample contg. one or more other serum lipoproteins and having a pH of 6.9-7.5, comprises (a) contacting the liq. sample with a solid support reagent contg. lectin attached to a solid support to bind lipoprotein (a) to the support-bound lectin, (b) removing lipoproteins in the sample which are not bound to the support and (c) assaying the lipoprotein (a) remaining.

The lectin may be e.g. wheat germ agglutinin (WGA), lima bean agglutinins, phytohaemagglutinin or horseshoe crab lectins. The assay for cholesterol may comprise **treating** the lipoprotein (a) with **cholesterol esterase** and a surfactant to release cholesterol and reacting the released cholesterol with cholesterol oxidase to produce H2O2 and assaying for H2O2 using a peroxidase enzyme.

USE/ADVANTAGE - The assays can be used for detecting elevated lipoprotein (a) levels in subjects with coronary artery disease or **atherosclerosis**. The purified lipoprotein (a) can be used for the prodn. of antibodies. The lectin binds specifically to lipoprotein (a) and allows specific assay and isolation. The methods can provide a direct lipoprotein (a) determn. and have a margin of error of +/- 1%.

Dwg.0/3

L11 ANSWER 15 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1994-031737 [04] WPIDS
DNC C1994-014534
TI Pancreatic lipase and cholesterol esterase inhibitors - contg protamine e.g. obtd from fish milt as active ingredient.
DC B04 D13
PA (CHOK-I) CHOKAN S
CYC 1
PI JP 05339168 A 19931221 (199404)* 8p
ADT JP 05339168 A JP 1992-147760 19920608
PRAI JP 1992-147760 19920608
AN 1994-031737 [04] WPIDS
AB JP 05339168 A UPAB: 19940307
Lipase activity in pancreatic juice and **cholesterol esterase** activity inhibitors comprise protamine as active ingredient. Also claimed is a food additive contg. protamine.

Protamine is obtd. from spermatozoon (milt) of fish and mammals such as herring, salmon, cod, mackerel, surgeon and carp, and chicken and mouse, and is pref. obtd. from fish spermatozoon (milt). Protamine is a strong basic simple protein with small molecular wt. and is easily dissolved in water, therefore, it is easily mixed with various food and formulated into various kinds of drugs.

USE/ADVANTAGE - The inhibitors delay the absorption of fat and cholesterol contained in food from the intestinal canal, therefore, it is useful for the prevention and **treatment** of adult diseases, esp. hyperlipaemia, and **arteriosclerosis**. The inhibitors and food additive contg. protamine reacts with micelles which are formed with bile acid and phospholipid and therefore, they do not cause any adverse effects.

Dwg.0/2

L11 ANSWER 16 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1992-415936 [50] WPIDS
CR 1994-191540 [23]
DNN N1992-317142 DNC C1992-184626
TI Assay for lipoprotein (A) in the presence of other lipoprotein(s) - comprises using lectin attached to a solid support to selectively bind the lipoprotein(A).
DC B04 S03
IN SEMAN, L J
PA (SEMA-I) SEMAN L J
CYC 17
PI WO 9221015 A1 19921126 (199250)* EN 23p
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: JP NO
EP 585387 A1 19940309 (199410) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
EP 585387 A4 19950118 (199545)
EP 585387 B1 19990811 (199936) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
DE 69229784 E 19990916 (199944)
ADT WO 9221015 A1 WO 1992-US4302 19920521; EP 585387 A1 EP 1992-913182 19920521, WO 1992-US4302 19920521; EP 585387 A4 EP 1992-913182 ; EP 585387 B1 EP 1992-913182 19920521, WO 1992-US4302 19920521; DE 69229784 E DE 1992-629784 19920521, EP 1992-913182 19920521, WO 1992-US4302 19920521
FDT EP 585387 A1 Based on WO 9221015; EP 585387 B1 Based on WO 9221015; DE 69229784 E Based on EP 585387, Based on WO 9221015
PRAI US 1991-704457 19910523
AN 1992-415936 [50] WPIDS
CR 1994-191540 [23]
AB WO 9221015 A UPAB: 19991026
A method is claimed for assaying lipoprotein (a) (LPa) in a liq. sample contg. one or more other serum LPs, comprising (a) contacting the liquid sample with a solid-support reagent contg. lectin attached to a solid support under conditions effective to bind LPa to the support bound lectin, (b) removing LPs in the sample which are not bound to the support and (c) assaying the LPa remaining after the removal.

Pref. the lictin binds specifically to LPa monosaccharide units selected from N-acetyl-D-glucosamine and N-acetylneuroaminic acid. The lectin may be e.g. wheat germ agglutinin, lima bean agglutinins, phytohaemagglutinin or horseshoe crab lectins. The assaying may include (i) **treating** the LPa with **cholesterol esterase** and a surfactant to release cholesterol from the LPa, (ii) reacting the released cholesterol with cholesterol oxidase to produce H2O2 and (iii) assaying for produced H2O2 using a peroxidase enzyme.

USE/ADVANTAGE - The assay method provides a direct LPa cholesterol determn. with a margin of error of + or - 1% for use in screening for coronary artery disease and advanced **atherosclerosis**.

3/3

Dwg.3/3

Dwg.3/3

L11 ANSWER 17 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1992-133595 [17] WPIDS
DNC C1992-062469
TI New tri cyclic heterocyclic derivs. are ACAT inhibitors - used for treating hypercholesterolaemia, atherosclerosis, myocardial infarction etc..
DC B02
IN IKEDA, H; MEGURO, K; TAWADA, H
PA (TAKE) TAKEDA CHEM IND LTD
CYC 17
PI EP 481243 A 19920422 (199217)* EN 34p
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
CA 2052287 A 19920328 (199223)
JP 05009179 A 19930119 (199311) 21p
US 5264454 A 19931123 (199348) 19p
US 5418239 A 19950523 (199526) 18p
ADT EP 481243 A EP 1991-116099 19910921; CA 2052287 A CA 1991-2052287 19910926; JP 05009179 A JP 1991-202003 19910812; US 5264454 A US 1991-765182 19910925; US 5418239 A Div ex US 1991-765182 19910925, US 1993-117950 19930908
FDT US 5418239 A Div ex US 5264454
PRAI JP 1990-259657 19900927; JP 1991-202003 19910812
AN 1992-133595 [17] WPIDS
AB EP 481243 A UPAB: 19931006
Fused heterocycle derivs. of formula (I) and their salts are new. Ring A and ring B= opt. substd. benzene; X= N(O)m= C(R2), N(R3)-CO or O-CO; R2= H, alkyl or alkoxy; m= 0-1; R3= H or alkyl; Y= bond, NH, 1-2C alkylene or vinylene; R1= opt. substd. hydrocarbyl; n= 3-6. Ring A and ring B= benzene opt. substd. by 1-4 of halo, 1-6C alkyl (opt. substd. by halo), 1-6C alkoxy (opt. substd. by halo), 1-6C alkylthio (opt. substd. by halo), 1-3C acyloxy, di(1-6C alkyl); amino or OH (esp. A=benzene substd. by 1-3 of halo, 1-6C alkyl or OH and B= benzene). X= N= CR2, NR3CO or OCO, R2= H or 1-6C alkoxy; R3= 1-6C alkyl; Y= NH or 1-2C alkylene; R1= 1-8C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl-(1-4C) alkyl, 6-10C aryl or 7-16C aralkyl all opt. substd. by 1-5 of halo, 1-6C alkyl (opt. substd. by halo), 1-6C alkoxy, (opt. substd. by halo), 1-6C alkylthio (opt. substd. by halo), 1-3C acyloxy, di(1-6C alkyl) amino or OH (esp. phenyl substd. by 1-3 of halo, 1-6C alkyl, 1-6C alkoxy, 1-6C acyloxy (sic), di(1-6C alkyl)amino or H (partic. 2,4-difluorophenyl)). n=3.
USE - (I) are acyl-CoA:cholesterol acyl transferase (ACAT) inhibitors ACAT inhibitors inhibit the absorption of dietary cholesterol from the intestinal tract, suppress the increase in cholesterol levels in the blood and suppress the accumulator of intracellular cholesterol. (I) are useful for treating hypercholesterolaemia and atherosclerosis and diseases associated with them e.g. ischaemic heart disease such as myocardial infarction and cerebrovascular disorders such as cerebral infarction and cerebral apoplexy). (0/0)
0/0
ABEQ US 5264454 A UPAB: 19940120
Heterocyclic derivs. of formula (I) and their salts are new; in which benzene rings A and B are opt. substd. by 1-4 of halo, opt. halogenated 1-6C alkyl, opt. halogenated 1-6C alkoxy, opt. halogenated 1-6C alkylthio, 1-3C acyloxy, di-(1-6C alkyl)amino and OH; X is -O-CO-; Y is a bond, NH or CHCH; R1 is 1-8C alkyl, 3-7C cycloalkyl, (3-7C cycloalkyl)-(1-4C alkyl), 1-6C aryl or 7-6C aralkyl opt. substd. by 1-5 of halo, opt. halogenated (1-6C alkyl, 1-6C alkoxy or 1-6C alkylthio), 1-3C acyloxy, di-(1-6C alkyl)amino and OH; n is 3, 4, 5, 6.
(I) is specifically N-(2,4-difluorophenyl)- N'(4-(2-methylphenyl)-2-oxo-2,6,7,8- tetrahydrocyclopenta (g)(1)benzo- pyran-3-yl) urea.
USE/ADVANTAGE - (I) are acyl-CoA:cholesterol acyltransferase inhibitors useful for prevention and **treatment** of hypercholesterolemia, **atherosclerosis**, ischaemic heart diseases, including myocardial infarction, and cerebrovascular disorders, including

cerebral infarction and cerebral apoplexy.
Dwg. 0/0

ABEQ US 5418239 A UPAB: 19950705
Heterocyclic cpds. of formula (I) and their salts are new: where n is 3-6; benzene rings A and B are opt. substd. by 1-4 of:1 halogen, or 1-6C alkyl, 1-6C alkoxy or 1-6C alkylthio, each opt. halogenated, or 1-3C acyloxy, di-(1-6C alkyl)amino or OH; X is -N(O)m=C(R2)- (in which m is 0 or 1; R2 is H, alkyl or alkoxy), or is -N(R3)-CO- (in which R3 is H or alkyl); Y is a bond, -NH-, 1 or 2C alkylene or -CH=CH-; R1 is 1-8C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl(1-4C alkyl), 6-10C aryl or 7-16C aralkyl, each opt. substd. by 1-5 of the substits. as for A and B.
N-(4-(2-Chlorophenyl)- 7,8-dihydro-6H-cyclopenta (g)quinolin-3-yl)-N'-(2,4-difluorophenyl)urea is specifically claimed.
USE - Acyl-CoA:**cholesterase** acyltransferase (ACAT) inhibitor comprises comprising a cpd. (I) and a carrier are claimed, and can be given to a mammal to **treat** hypercholesterolaemia, **atherosclerosis**, heart diseases and cerebrovascular disorders.
Dwg.0/0

L11 ANSWER 18 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1991-150354 [21] WPIDS
DNC C1991-065001
TI 4-phenoxy phenyl carbamate ester derivs. - useful as **cholesterol ester hydrolase** inhibitors to **treat** coronary heart disease, **atherosclerosis**, etc..
DC B03 B05
IN COMMONS, T J; MEWSHAW, R E; STRIKE, D P; NEWSHAW, R E
PA (AMHP) AMERICAN HOME PROD CORP
CYC 10
PI

EP 428385	A	19910522	(199121)*	
GB 2238542	A	19910605	(199123)	
HU 55352	T	19910528	(199127)	
CA 2029934	A	19910516	(199130)	
FI 9005558	A	19910516	(199133)	
PT 95869	A	19910913	(199140)	
AU 9066534	A	19910718	(199141)	
JP 03206071	A	19910909	(199142)	
ZA 9009103	A	19920729	(199235)	71p
NZ 236061	A	19930225	(199312)	
AU 635087	B	19930311	(199317)	
HU 207842	B	19930628	(199332)	
GB 2238542	B	19930901	(199335)	
US 5391571	A	19950221	(199513)	16p
US 5512565	A	19960430	(199623)	12p
US 5602151	A	19970211	(199712)	11p

ADT EP 428385 A EP 1990-312382 19901113; GB 2238542 A GB 1990-24693 19901113; JP 03206071 A JP 1990-311216 19901115; ZA 9009103 A ZA 1990-9103 19901113; NZ 236061 A NZ 1990-236061 19901113; AU 635087 B AU 1990-66534 19901113; HU 207842 B HU 1990-7132 19901115; GB 2238542 B GB 1990-24693 19901113; US 5391571 A CIP of US 1989-436841 19891115, Cont of US 1990-594241 19901009, Cont of US 1991-771580 19911004, US 1993-62026 19930513; US 5512565 A CIP of US 1989-436841 19891115, Cont of US 1990-594241 19901009, Cont of US 1991-771580 19911004, Div ex US 1993-62026 19930513, Div ex US 1994-277396 19940719, US 1995-413559 19950330; US 5602151 A CIP of US 1989-436841 19891115, Cont of US 1990-594241 19901009, Cont of US 1991-771580 19911004, Div ex US 1993-62026 19930513, Div ex US 1994-277396 19940719, US 1995-572993 19951215
FDT AU 635087 B Previous Publ. AU 9066534; HU 207842 B Previous Publ. HU 55352; US 5512565 A Div ex US 5391571; US 5602151 A Div ex US 5391571
PRAI US 1990-594241 19901009; US 1989-436841 19891105; GB 1990-5537 19900312; US 1991-771580 19911004; US 1993-62026 19930513; US 1994-277396 19940719; US 1995-413559 19950330; US 1995-572993 19951215
AN 1991-150354 [21] WPIDS
AB EP 428385 A UPAB: 19930928

4-Phenoxyphenyl carbamate of formula (I) and their salts are new.
R1= opt. unsatd. 4-20C alkyl, 3-8C cycloalkyl, 1- or 2-adamantyl, 3-noradamantyl, 3-methyl-1-adamantyl, 1- or 9-fluorenyl, (3-8C cycloalkyl)-(1-6C alkyl), phenyl or phenyl-(1-20C alkyl). R2= H or 1-6C alkyl or R1 and R2 together form a heterocycle (i). X= -C(R7)(R8)-, NR9, O or S. R7= H, 1-6C alkyl, OH, 2-6C alkanoyloxy, 1-6C hydroxyalkyl, CO2H, 2-16C alkoxycarbonyl or phenyl. R8= H or 1-6C alkyl or R7 and R8 together are (CH2)m where m=2-6. R9= H, 1-6C alkyl, or phenyl, halo, NO2, or CN. R10= H, 1-6C alkyl or 2-12C gem-dialkyl. n=0,1 or 2. R3, R4, R5, R6= independently H, 1-6C alkyl, alkoxy, or perhaloalkyl halo, NO2, CN, CO2H or 2-16C alkoxycarbonyl. When X= NR9 or R7= aminoalkyl, (I) can be present in salt form.
USE/ADVANTAGE - As inhibitors of **cholesterol ester hydrolase**. (I) are therefore useful to **treat** coronary heart disease, . **atherosclerosis**, familial hypercholesterolaemia, hyperlipaemia, etc.
0/0

ABEQ GB 2238542 B UPAB: 19931119
A compound of the formula (I) in which R1 is branched or straight chain, saturated or unsaturated alkyl of 4 to 20 carbon atoms, cycloalkyl of 3 to 8 carbon atoms, 1-adamantyl, 2-adamantyl, 3-noradamantyl, 3-methyl-1-adamantyl, 1-fluorenyl, 9-fluorenyl, cycloalkylalkyl where the cycloalkyl moiety has 3 to 8 carbon atoms and the alkyl moiety has 1 to 6 carbon atoms, phenyl, substituted phenyl where the substituents are alkyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, halo, nitro, cyano or trifluoromethyl, phenylalkyl of 7 to 26 carbon atoms or substituted phenylalkyl, where the alkyl moiety is 1 to 20 carbon atoms and the substituent on the benzene ring is alkyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, halo, nitro, cyano, trifluoromethyl or phenyl; R2 is hydrogen, alkyl of 1 to 6 carbon atoms or R1 taken with R2 and the nitrogen atom to which they are attached form a heterocyclic moiety of the formula (II).
Dwg.0/0

ABEQ US 5391571 A UPAB: 19950404
Carbamate esters of formula (I) are new. In the formula, R is 4-20C-alkyl, or -alkenyl, 3-8C cycloalkyl, 1- and 2-adamantyl, 3-noradamantyl, 3-methyl-1-adamantyl, 1- and 9-fluorenyl, 3-8C cycloalkylalkyl, Ph opt substd; R2 is H or 1-6C alkyl; R3-R6 are each H, 1-6C-alkyl or -alkoxy, halo, NO2, CN, 1-6C perhaloalkyl, 2-16C alkoxycarbonyl or hydroxycarbonyl.
Specifically claimed cpds include butylcarbamic acid 4-phenoxyphenyl ester.
USE - (I) inhibit cholesterol ester hydrolase and reduce cholesterol absorption and are used to treat hypercholesterolaemia.
Dwg.0/0

ABEQ US 5512565 A UPAB: 19960610
A cpd. of formula (I) is new:
X = S;
n = 1;
R3-R6 = H, 1-6C alkyl, 1-6C alkoxy, halo, nitro, cyano or 1-6C perhaloalkyl, 2-16C alkoxycarbonyl or hydroxycarbonyl.
Dwg.0/0

ABEQ US 5602151 A UPAB: 19970320
A compound which is:
4-phenyl-1-piperidinecarboxylic acid 4-phenoxyphenyl ester;
4-methyl-1-piperidinecarboxylic acid 4-(4-methylphenoxy)phenyl ester;
4-methyl-1-piperidinecarboxylic acid 4-(4-chlorophenoxy)phenyl ester;
4-methyl-1-piperidinecarboxylic acid 4-(4-methoxyphenoxy)phenyl ester;
4-methyl-1-piperidinecarboxylic acid 2-bromo-4-phenoxyphenyl ester;
4,4-dimethyl-1-piperidinecarboxylic acid 4-phenoxyphenyl ester;
4-methyl-1-piperidinecarboxylic acid 2-fluoro-4-phenoxyphenyl ester;
4-ethyl-1-piperidinecarboxylic acid 4-phenoxyphenyl ester;
1,4-piperidinedicarboxylic acid 4-ethyl-1-(4-phenoxyphenyl) diester;
4-hydroxy-1-piperidinecarboxylic acid 4-phenoxyphenyl ester;
4-propyl-1-piperidinecarboxylic acid 4-phenoxyphenyl ester;

1,4-piperidinedicarboxylic acid 1-(4-phenoxyphenyl ester);
3,3-dimethyl-1-piperidinecarboxylic acid 4-phenoxyphenyl ester;
4-(acetyloxy)-1-piperidinecarboxylic acid 4-phenoxyphenyl ester;
4-methyl-1-piperidinecarboxylic acid 2-(methoxycarbonyl)-4-phenoxyphenyl ester;
4-(1-methylethyl)-1-piperidinecarboxylic acid 4-phenoxyphenyl ester;
1,4-piperidinedicarboxylic acid 4-dodecyl 1-(4-phenoxyphenyl) diester;
4-methyl-1-piperidinecarboxylic acid 2-cyano-4-phenoxyphenyl ester;
4-methyl-1-piperidinecarboxylic acid 2-(hydroxycarbonyl)-4-phenoxyphenyl ester;
4-(hydroxymethyl)-1-piperidinecarboxylic acid 4-phenoxyphenyl ester;
4-(bromomethyl)-1-piperidinecarboxylic acid, 4-phenoxyphenyl ester;
4-methyl-1-piperidinecarboxylic acid 2-(dodecyloxycarbonyl)-4-phenoxyphenyl ester;
4-(iodomethyl)-1-piperidinecarboxylic acid 4-phenoxyphenyl ester;
4-(diethylaminomethyl)-1-piperidinecarboxylic acid 4-phenoxyphenyl ester;
1-[(4-phenoxyphenoxy)carbonyl]-4-piperidinemethanaminium iodide;
4-(dihexylaminomethyl)-1-piperidinecarboxylic acid 4-phenoxyphenyl ester; or
2-methyl-1-piperidinecarboxylic acid 4-phenoxyphenyl ester; or a pharmaceutically acceptable salt.
Dwg.0/0

L11 ANSWER 19 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1990-218740 [29] WPIDS
DNN N1990-169759 DNC C1990-094452
TI Determn. of net high density lipoprotein cholesterol content of serum - by pptn. of other lipoprotein(s) then assaying cholesterol in lipase treated and untreated samples, for assessing risk of vascular disease.
DC B04 D13 S03
IN MAINES, R Q
PA (MAIN-I) MAINES R Q
CYC 14
PI EP 378395 A 19900718 (199029)*
R: AT BE CH DE ES FR GB LI LU NL SE
CA 2007645 A 19900713 (199039)
EP 378395 A3 19920701 (199333)
US 5453358 A 19950926 (199544) 5p
EP 378395 B1 19960814 (199637) EN 12p
R: AT BE CH DE DK ES FR GB LI LU NL SE
DE 69028023 E 19960919 (199643)
ADT EP 378395 A EP 1990-300287 19900110; EP 378395 A3 EP 1990-300287 19900110; US 5453358 A Cont of US 1989-297080 19890113, US 1992-941669 19920908; EP 378395 B1 EP 1990-300287 19900110; DE 69028023 E DE 1990-628023 19900110, EP 1990-300287 19900110
FDT DE 69028023 E Based on EP 378395
PRAI US 1989-297080 19890113; US 1992-941669 19920908
AN 1990-218740 [29] WPIDS
AB EP 378395 A UPAB: 19931119
Determin. of the net HDL cholesterol content of blood serum comprises (1) treating a sample with a pptg. agent which combines with LDL and VLDL particles in the serum; (2) centrifuging to remove ppte., leaving supernatant contg. HDL and free cholesterol (ch); (3) treating supernatant with enzyme which de-esterifies (ch), so as to break down HDL particles into (Ch) and fatty acid; (4) treating with (Ch) oxidase to oxidise all (Ch)to H2O2 and cholest-4-en-3-one; (5) treating with peroxidase (POD), 4-amine-antipyrine (4AAP) and chromogen to convert the H2O2 producedto a quinone imine (QI); (6) measuring the absorbance of QI at a suitable wavelength; (7) repeating steps (3-6) on at least one (Ch)-contg. standard; (8) calculating the concn. of HDL and non-pptd. (Ch) from the equation (HDL + free (Ch) concn.) = S.C. x 2As/Ast. (As and Ast = absorbance of sample and standard respectively; S.C = concn. of the standard); (9) repeating steps (4-6) on separate samples of supernatant

and standard, (10) calculating the non-pptd. free (Ch) concn. from the eqn. free (Ch) concn. = S.C. x 2As/Ast and (11) calculating net HDL cholesterol by subtraction of results from steps (8) and (10).

Also new is an emulsified diet supplement for increasing % HDL cholesterol in the blood consisting of a polyunsatd. lipid, phospholipid contg. essential fatty acids; a polysaccharide and an antioxidant.

USE - The measurement of HDL cholesterol is used to diagnose (and assess the risk of) vascular disease and atherosclerosis. The new diet supplement reduces the risk of such diseases. @(9pp Dwg.No.0/0)

0/0

ABEQ US 5453358 A UPAB: 19951109

Determining the level of risk for a patient to vascular disease comprises (a) determining the net percentage of HDL cholesterol of blood serum by (i) precipitating LDL and VLDL fractions from a blood serum sample, (ii) sepg. and isolating the precipitant from a supernatant, (iii) **treating** the supernatant with **cholesterol esterase** or lipase to de-esterify HDL cholesterol, (iv) converting all of the cholesterol in the supernatant to H2O2 and cholest-4-en-3-one, (v) converting all H2O2 to quinoneimine in the supernatant, (vi) determining the amt. of quinoneimine in the supernatant, (vii) converting the amt. into a concn. of HDL cholesterol and free cholesterol, (viii) effecting steps (iv)-(vi) on a 2nd sample of the supernatant from step (ii) and converting the amt. into a concn. of free cholesterol, and (ix) determining net HDL cholesterol by subtracting the concn. of free cholesterol from step (viii) from the concn. of HDL cholesterol and free cholesterol from step (vii), and (b) determining an increased risk of vascular disease for patients exhibiting concns. of net HDL cholesterol that are less than 15% of total serum cholesterol.

USE - The method is also used for diagnosing **atherosclerosis**.

Dwg.0/0

ABEQ EP 378395 B UPAB: 19960918

A method of determining the net concentration of cholesterol associated with HDL particles in blood serum, comprising the steps of (a) **treating** a sample of the serum with a precipitating agent which will combine with the LDL and VLDL particles in the serum; (b) centrifuging the **treated** serum sample until the LDL- and VLDL-containing precipitate is spun down, leaving a supernatant liquid having HDL associated cholesterol, and free supernatant cholesterol; (c) separating the supernatant liquid from the precipitate; (d) **treating** a fist sample of the supernatant liquid with **cholesterol esterase** or lipase in sufficient quantity to break down all the HDL particles into fee cholesterol and fatty acids, resulting in a cholesterol-containing fluid having no esterified cholesterol; (e) **treating** the cholesterol-containing fluid with cholesterol oxidase in sufficient quantity to oxidise all the cholesterol present, forming hydrogen peroxide and cholest-4-en-3-one; (f) further **treating** the fluid with peroxidase, 4-aminoantipyrine and a chromogen in sufficient amounts to completely react all the hydrogen peroxide formed in step (e) to produce a quinoneimine; (g) measuring the electromagnetic radiation absorbance of the quinonimine-containing fluid produced in step (h) at a wavelength at which the quinonimine exhibits significant absorbance; (i) performing steps (d) through (g) on each of one or more standard cholesterol-containing fluids; (j) calculating the combined concentration of cholesterol associated with the HDL particles, and free supernatant cholesterol according to the formula (cholesterol associated with HDL + free supernatant cholesterol concentration) = standard concentration x 2(Asupernatant)/A standard, where Asupernatant represents the absorbance measured for the supernatant and Astandard represents the absorbance measured for the standard cholesterol-containing fluid; (k) performing steps (e) through (g) on a second sample of the supernatant liquid, and one or more standard cholesterol-containing fluids, (l) calculating the concentration of free supernatant cholesterol from the absorbance values obtained in step (j) according to the formula free supernatant cholesterol concentration = 2(Asupernatant)/Astandard x

standard concentration; and (m) calculating the net concentration of cholesterol associated with HDL particles from the results of steps (i) and (k) according to the formula net concentration of cholesterol associated with HDL = (cholesterol associated with HDL + free supernatant cholesterol concentration) - free supernatant cholesterol concentration.
Dwg.0/0

L11 ANSWER 20 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1988-269131 [38] WPIDS
DNN N1988-204158 DNC C1988-120103
TI Lipid analysis in blood serum or plasma - involves liq. chromatography and preliminary enzymatic hydrolysis of stabilising proteins, to increase accuracy.
DC B04 D16 S03
IN DVORKIN, V I; VAVKUSHEVS, I N; ZOLOTOV, N N
PA (AMCA-R) A MED CARDIOL CENTR
CYC 1
PI SU 1377733 A 19880229 (198838)* 3p
ADT SU 1377733 A SU 1985-3922509 19850704
PRAI SU 1985-3922509 19850704
AN 1988-269131 [38] WPIDS
AB SU 1377733 A UPAB: 19930923
To determine glycerides **treatment** (of the sample) involves phospholipase. To determine ethers (
) of cholesterol and steroids **treatment** involves lipase. To determine phospholipides **treatment** involves **cholesterol -esterase**. As previously, the method involves:- extg. lipids by an organic solvent; liq. chromatography.
USE/ADVANTAGE - Increased accuracy in the analysis of lipids in blood serum or plasma in biochemistry and medical practice, esp. in investigation of lipid exchange and pathogenesis of **atherosclerosis**. Typically, in analysis of cholesterol ethers the proposed method reduces the error from 100+% to 4-6%. In analysis of acyglycerol the proposed method reduces error from 10-12% to 5-6%.
Bul.8/29.2.88.
0/0

L11 ANSWER 21 OF 68 WPIDS (C) 2003 THOMSON DERWENT
AN 1988-121051 [18] WPIDS
DNN N1988-091887 DNC C1988-054205
TI Specific measurement of high density lipoprotein cholesterol in serum - by incubation with esterase and oxidase, and kinetic monitoring of hydrogen peroxide formation.
DC A96 B04 D16 S03
IN KERSCHER, L; PAUTZ, B; TRUNK, G; ZIEGENHORN, J
PA (BOEF) BOEHRINGER MANNHEIM GMBH; (BOEF) OEHRINGER MANNHEIM GMBH
CYC 20
PI EP 265933 A 19880504 (198818)* DE 16p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 3636851 A 19880511 (198820)
AU 8780446 A 19880505 (198826)
JP 63126498 A 19880530 (198827)
FI 8704749 A 19880430 (198831)
US 4892815 A 19900109 (199010) 11p
CA 1309645 C 19921103 (199250)
EP 265933 B1 19930203 (199305) DE 19p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 3784004 G 19930318 (199312)
FI 90882 B 19931231 (199404)
JP 07034760 B2 19950419 (199520) 10p
ADT EP 265933 A EP 1987-115841 19871028; DE 3636851 A DE 1986-3636851 19861029; JP 63126498 A JP 1987-269522 19871027; US 4892815 A US 1987-107467 19871006; CA 1309645 C CA 1987-549035 19871009; EP 265933 B1 EP 1987-115841 19871028; DE 3784004 G DE 1987-3784004 19871028, EP 1987-115841 19871028; FI 90882 B FI 1987-4749 19871028; JP 07034760 B2 JP

1987-269522 19871027
FDT DE 3784004 G Based on EP 265933; FI 90882 B Previous Publ. FI 8704749; JP 07034760 B2 Based on JP 63126498
PRAI DE 1986-3636851 19861029
AN 1988-121051 [18] WPIDS
AB EP 265933 A UPAB: 19950530
Specific determination of HDL-cholesterol in presence of the LDL fraction of serum lipoproteins comprises treating with cholesterol esterase (CE) to release cholesterol which is oxidised with cholesterol oxidase (CO) and O2 to form H2O2, then kinetic measurement of H2O2 formation or of O2 consumption.

The new feature is that measurement is carried out at 2-15 min after start of oxidase reaction at 20-40 deg C for a predetermined time interval. During measurement concns maintained in the reaction soln are: CE 0.05-30 u/ml; Co 0.1-50 U/ml; bile acid surfactant 1-20 mM and nonionic surfactant 0.1-10 g/l, while pH is 5-9. Also new is a reagent which provides the specified concns. of CO, CE and surfactants, plus pH 5-9 buffer and a system for photometric measurement of H2O2.

ADVANTAGE - The HDL component is measured with a simple reagent in a single step, and the same sample can also be used to provide a measure of total cholesterol.

0/5

Dwg.0/5

ABEQ EP 265933 B UPAB: 19930923
Process for the specific determination of the cholesterol of the HDL fraction in the presence of the LDL fraction of the lipoproteins of the serum by action of **cholesterol esterase** for the liberation of the cholesterol and oxidation of the liberated cholesterol with cholesterol oxidase and oxygen with the formation of H2O2 and kinetic measurement of the H2O2 formation or of the oxygen consumption, characterised in that one uses the **cholesterol esterase** from pancreas and that the measurement is carried out within 2 minutes to 15 minutes after the start of the oxidase reaction at a temperature of 20 to 40 deg.C during a predetermined time interval and during the measurement there is maintained in the reaction solution a **cholesterol esterase** concentration of 0.05 to 30 U/ml, a cholesterol oxidase concentration of 0.1 to 50 U/ml, a concentration of a tenside of the bile acid group of 1.0 to 20 mMol/l, a concentration of a non-ionic detergent of 0.1 to 10 g/l and a pH value of 5 to 9.

0/5

ABEQ US 4892815 A UPAB: 19930923
High density lipoprotein (HDL) cholesterol is specifically determined in a serum lipoprotein contg. low density lipoprotein (LDL) in a sample, by adding (i) pancreatic **cholesterol esterase** to liberate cholesterol from its esters; (ii) cholesterol oxidase and O2 to oxidise liberated cholesterol and form H2O2; and (iii) kinetically measuring H2O2-formation or O2-consumption within 2-15 mins. as a measurement of HDL cholesterol.

Measurement and reaction take place at 20-40 deg.C during a predetermined time interval using a maintained esterase concn. of 0.05-30 U per ml., oxidase concn. of 0.1-50 U per ml., tenside of bile acid gp. at 1.0-20 mmol. per l., and 0.1-10 g per l. of non-ionic detergent at pH 5-9.

USE - In **treatment** of hypercholesterolaemic and hypertriglyceridaemia in **atherosclerosis** or cardiac infarct.

L11 ANSWER 22 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 2001:581727 CAPLUS
DN 135:147445
TI Use of **lysosomal acid lipase** for **treating atherosclerosis** and related diseases
IN Grabowski, Gregory A.; Du, Hong
PA Children's Hospital Research Foundation, USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001056596	A1	20010809	WO 2001-US3481	20010202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2001008077	A	20021022	BR 2001-8077	20010202
EP 1267914	A1	20030102	EP 2001-906927	20010202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI US 2000-180362P	P	20000204		
US 2001-775517	A	20010202		
WO 2001-US3481	W	20010202		

AB The present invention comprises a method to diminish and/or eliminate atherosclerotic plaques, in mammals, through direct and indirect treatment of these plaques, in situ, using suitable substances which are capable of lipid removal, primarily through hydrolysis, either by a catalytic or stoichiometric process, wherein the substance targets receptors in and/or on the cell which lead to uptake into the lysosome. Such substances used to diminish and/or eliminate atherosclerotic plaques are generally comprised of lipid hydrolyzing proteins and/or polypeptides.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 23 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 2000:812199 CAPLUS
DN 134:69432
TI Aggregation, fusion, and vesicle formation of modified low density lipoprotein particles: molecular mechanisms and effects on matrix interactions
AU Oorni, Katariina; Pentikainen, Markku O.; Ala-Korpela, Mika; Kovanen, Petri T.
CS Wihuri Research Institute, Helsinki, FIN-00140, Finland
SO Journal of Lipid Research (2000), 41(11), 1703-1714
CODEN: JLPRAW; ISSN: 0022-2275
PB Lipid Research, Inc.
DT Journal; General Review
LA English
AB A review with 148 refs. Initiation of **atherosclerosis** is characterized by accumulation of aggregates of small lipid droplets and vesicles in the extracellular matrix of the arterial intima. The droplets and vesicles have features that suggest that they are formed from modified plasma-derived low d. lipoprotein (LDL) particles. A variety of hydrolytic enzymes and prooxidative agents that could lead to extracellular assembly of LDL-derived droplets and vesicles are present in the arterial intima. In fact, in vitro studies have demonstrated that extensive oxidn. of LDL and **treatment** of LDL with either proteolytic or lipolytic enzymes will induce LDL aggregation and fusion and **treatment** of LDL with **cholesterol esterase** will cause formation of vesicles. Fusion of LDL particles proceeds faster in vitro when they are bound to components of the extracellular matrix derived from the arterial intima, such as proteoglycans, and, depending on the type of modification, the strength of binding of modified LDL to the matrix components may either increase or decrease. In the present article, we discuss mol. mechanisms that provide clues as to how aggregated lipid droplets and vesicles may be derived from modified LDL

particles. We also describe how these modified forms of LDL, by means of their trapping to the extracellular matrix, may lead to extracellular lipid accumulation in the arterial intima.

RE.CNT 148 THERE ARE 148 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 24 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 2000:65106 CAPLUS
DN 132:217431
TI Prostaglandin E1 influences serum cholesterol esterase and lipase activity in different ways
AU Piorunska-Stolzmann, M.
CS Clinical Biochemistry, Department of General Chemistry, Karol Marcinkowski University of Medical Sciences, Poznan, Pol.
SO International Journal of Tissue Reactions (1999), 21(3), 79-83
CODEN: IJTEDP; ISSN: 0250-0868
PB Bioscience Ediprint Inc.
DT Journal
LA English
AB The in vitro and in vivo effects of prostaglandin E1 on **cholesterol ester hydrolase** (CEase) and lipase [glycerol ester hydrolase (GEH)] activity in human serum were examd. **Cholesterol esterase** and lipase activity in the sera of men with **atherosclerosis** differed substantially from that in the control subjects. CEase activity was raised and GEH activity suppressed in the serum of men with **atherosclerosis** compared with controls. Prostaglandin E1 in vitro was found to suppress lipase but to increase **cholesterol esterase** activity to some extent. However, in vivo activities of GEH and CEase in the sera of men with chronic arterial occlusions of the lower limbs **treated** with prostaglandin E1 revealed that lipase activity was increased but that **cholesterol esterase** activity was unchanged. Recent studies have demonstrated that by altering the metabolic pathways of acylcholesterols and triacylglycerols, prostaglandin E1 may lead to the development of new strategies for retarding **atherosclerosis**.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1998:412362 CAPLUS
DN 129:197833
TI Hormone-sensitive lipase overexpression increases cholesteryl ester hydrolysis in macrophage foam cells
AU Escary, Jean-Louis; Choy, Henry A.; Reue, Karen; Schotz, Michael C.
CS Lipid Research Laboratory, West Los Angeles VA Medical Center, University of California, Los Angeles, CA, 90073, USA
SO Arteriosclerosis, Thrombosis, and Vascular Biology (1998), 18(6), 991-998
CODEN: ATVBFA; ISSN: 1079-5642
PB Williams & Wilkins
DT Journal
LA English
AB **Atherosclerosis** is a complex physiopathol. process initiated by the formation of cholesterol-rich lesions in the arterial wall. Macrophages play a crucial role in this process because they accumulate large amts. of cholesterol esters (CEs) to form the foam cells that initiate the formation of the lesion and participate actively in the development of the lesion. Therefore, prevention or reversal of CE accumulation in macrophage foam cells could result in protection from multiple pathol. effects. In this report, we show that the CE hydrolysis catalyzed by neutral **cholesterol ester hydrolase** (nCEH) can be modulated by overexpression of hormone-sensitive lipase (HSL) in macrophage foam cells. For these studies, RAW 264.7 cells, a murine macrophage cell line, were found to be a suitable model of foam cell formation. HSL expression and nCEH activity in these cells and in peritoneal macrophages were comparable. In addn.,

antibody titrn. showed that essentially all nCEH activity in murine macrophages was accounted for by HSL. To examine the effect of HSL overexpression on foam cell formation, RAW 264.7 cells were stably transfected with a rat HSL cDNA. The resulting HSL overexpression increased hydrolysis of cellular CEs 2- to 3-fold in lipid-laden cells in the presence of an acyl CoA:cholesterol acyltransferase (ACAT) inhibitor. Furthermore, addn. of cAMP produced a 5-fold higher rate of CE hydrolysis in cholesterol-laden, HSL-overexpressing cells than in control cells and resulted in nearly complete hydrolysis of cellular CEs in only 9 h, compared with <50% hydrolysis in control cells. Thus, HSL overexpression stimulated the net hydrolysis of CEs, leading to faster hydrolysis of lipid deposits in model foam cells. These data suggest that HSL overexpression in macrophages, alone or in combination with ACAT inhibitors, may constitute a useful **therapeutic** approach for impeding CE accumulation in macrophages in vivo.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 26 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1998:466751 CAPLUS
DN 129:273975
TI Cholesteryl esterase-treated LDL augments oxidized LDL-mediated cholesteryl ester deposition in mouse peritoneal macrophages
AU Yu, Hong; Gutman, Robert L.; Ryu, Beung-Ho; Greenspan, Phillip
CS College of Pharmacy, Department of Pharmaceutical and Biomedical Sciences, University of Georgia, Athens, GA, 30602, USA
SO Atherosclerosis (Shannon, Ireland) (1998), 140(1), 35-43
CODEN: ATHSBL; ISSN: 0021-9150
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB Arterial unesterified cholesterol, phospholipid particles have been isolated from atherosclerotic lesions and characterized. However, the role of these 'liposomes' in macrophage foam cell formation is unclear. Recently, LDL, after trypsin and cholesteryl esterase treatment (T/CE LDL), was shown to have phys. properties similar to the unesterified cholesterol, phospholipid particles isolated from atherosclerotic lesions. Yet, when mouse peritoneal macrophages were incubated with these model particles in culture medium (DMEM and 5% LPDS), only an insignificant accumulation of cellular cholesteryl esters was obsd. Previously, the authors demonstrated that complex formation between unesterified cholesterol, phosphatidylcholine liposomes and cupric sulfate-oxidized LDL dramatically enhances the ability of the liposomes to augment cellular cholesterol accretion (Greenspan P, Yu H, Mao F, Gutman RL. J Lipid Res 1997;38:101-109). When T/CE LDL, another cholesterol-rich phospholipid particle, was substituted for unesterified cholesterol phosphatidylcholine liposomes in the complex, mouse peritoneal macrophages accumulated a significant amt. of both cellular unesterified cholesterol (61 .mu.g/mg cell protein) and cholesteryl esters (76 .mu.g/mg cell protein) after 48 h of incubation. These results demonstrate again that the interaction of two cholesterol-bearing particles (T/CE LDL and oxidized LDL), which individually can not promote significant cholesterol accumulation in cells, will, when combined, produce macrophage foam cells.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 27 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1997:338577 CAPLUS
DN 126:312696
TI Wolman disease
AU Yatsu, Frank M.; Alam, Rita
CS University of Texas Houston Medical School, Houston, TX, USA
SO Molecular and Genetic Basis of Neurological Disease (2nd Edition) (1997), 371-378. Editor(s): Rosenberg, Roger N. Publisher: Butterworth-Heinemann, Boston, Mass.

CODEN: 64KBAL
DT Conference; General Review
LA English
AB A review with 30 refs. Wolman disease (WD) and cholesteryl ester storage disease (CESD) result from a deficiency of human lysosomal cholesteryl ester lipase (HLAL)/**lysosomal acid lipase** (LIPA)/**cholesteryl ester hydrolase** (CEH) that causes an abnormal accumulation of cholesteryl esters and triglycerides in tissues. WD commences in infancy and is usually fatal during that period, whereas CESD starts in childhood and adulthood and may be clin. benign. Diagnosis can be made prenatally using cultured cells from amniocentesis or chorionic villus cells. The enzyme level can be quantitated using various lipid substrates such as radiolabeled cholesterol oleate, 14C-triolein, and esters of 4-methylumbelliferyl palmitate and p-nitrophenol. Postparturition, leukocytes, and urinary sediment can be assayed to make the diagnosis. **Therapy** to reconstitute the reduced enzyme with bone marrow transplantation has been attempted, although to data direct transfer of the gene has not. Recent mol. biol. studies have localized the WD/CESD enzyme to chromosome 10q23.2-q23.3, and the genomic sequences encoding lysosomal **cholesterol ester hydrolase**/LIPA (**sterol esterase** 3.1.1.13) have been isolated and sequenced, with identification of the gene defects in WD. The gene is 36 kb long and has 10 exons. The mutations are a T insertion after position 634, resulting in an in-frame translation stop signal 13 codon downstream and a T-to-C transition at nucleotide 638. This mutation results in a leucine-to-proline substitution at amino acid 179 and alters the alpha-helical structure of the protein. Both mutations impair the enzyme's function. Future studies on these genes and advances in gene transfer technol. offer the prospect of benefiting patients with these diseases. In addn., the potential role of this enzyme in **atherosclerosis** can be clarified. WD, like CESD, results from an autosomal recessive inheritance of the deficiency of HLAL or LIPA (**sterol esterase** [EC] 3.1.1.13). This deficiency causes an accumulation in tissues of cholesteryl esters and triglycerides. WD differs from CESD in commencing in infancy with death during that period, whereas CESD begins in childhood or adulthood and has a more benign clin. course [1-6]. Recent mol. biol. studies have isolated and sequenced this gene, and the specific defects in WD have been identified, as discussed below. These rapidly advancing discoveries on the fundamental defects in WD and CESD and those on the technol. of gene transfer into cells promise to shed light on practical means of complementing or correcting the defective gene.

L11 ANSWER 28 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1996:466972 CAPLUS
DN 125:109645
TI Method for detecting HDL-cholesterol in blood serum or plasma
IN Majima, Hatsuichi; Asano, Shigeki; Kikuchi, Toshiro; Kawamura, Yoshihisa
PA Toyo Boseki, Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08116996	A2	19960514	JP 1994-262679	19941026
PRAI	JP 1994-262679		19941026		

AB The HDL-cholesterol detn. method comprises sepn. of lipoprotein fraction, **treatment** of sample with anionic surfactant and **cholesterol esterase** and cholesterol oxidase, and measurement of hydrogen peroxide formation. The anionic surfactant is selected from alkyl sulfonate salt, bile acid, or derivs., and fractionation agent is selected from dextran sulfate, heparin, sodium

phosphotungstate, or amylopectin sulfate, or their salts. Both **cholesterol esterase** and oxidase are oligo-glucose-modified or derivatized oxidase and esterase. 4-Aminoantipyrine and peroxidase are used in hydrogen peroxide detn. The method is useful for prognosis of coronary **atherosclerosis**.

L11 ANSWER 29 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1995:978593 CAPLUS
DN 124:27072
TI On the pathogenesis of atherosclerosis: enzymic transformation of human low density lipoprotein to an atherogenic moiety
AU Bhakdi, Sucharit; Dorweiler, Bernhard; Kirchmann, Roger; Torzewski, Jan; Weise, Eric; Tranum-Jensen, Joergen; Walev, Iwan; Wieland, Eberhard
CS Institute of Medical Microbiology and Hygiene, University of Mainz, Mainz, D-55101, Germany
SO Journal of Experimental Medicine (1995), 182(6), 1959-71
CODEN: JEMEAV; ISSN: 0022-1007
PB Rockefeller University Press
DT Journal
LA English
AB Combined **treatment** with trypsin, **cholesterol esterase**, and neuraminidase transforms LDL, but not HDL or VLDL, to particles with properties akin to those of lipid extd. from atherosclerotic lesions. Single or double enzyme modifications, or **treatment** with phospholipase C, or simple vortexing are ineffective. Triple enzyme **treatment** disrupts the ordered and uniform structure of LDL particles, and gives rise to the formation of inhomogeneous lipid droplets 10-200 nm in diam. with a pronounced net neg. charge, but lacking significant amts. of oxidized lipid. Enzymically modified LDL (E-LDL), but not oxidatively modified LDL (ox-LDL), is endowed with potent complement-activating capacity. As previously found for lipid isolated from atherosclerotic lesions, complement activation occurs to completion via the alternative pathway and is independent of antibody. E-LDL is rapidly taken up by human macrophages to an extent exceeding the uptake of acetylated LDL (ac-LDL) or oxidatively modified LDL. After 16 h, cholesteryl oleate ester formation induced by E-LDL (50 .mu.g/mL cholesterol) was in the range of 6-10 nmol/mg protein compared with 3-6 nmol/mg induced by an equiv. amt. of acetylated LDL. At this concn., E-LDL was essentially devoid of direct cytotoxic effects. Competition expts. indicated that uptake of E-LDL was mediated in part by ox-LDL receptor(s). Thus, .apprx.90% of 125I-ox-LDL degrdn. was inhibited by a 20-fold excess of unlabeled E-LDL. Uptake of 125I-LDL was not inhibited by E-LDL. The authors hypothesize that extracellular enzymic modification may represent an important step linking subendothelial deposition of LDL to the initiation of **atherosclerosis**.

L11 ANSWER 30 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1994:498900 CAPLUS
DN 121:98900
TI Biochemical mechanisms associated with the lipolytic effects of calcium channel blockers
AU Pomerantz, Kenneth B.; Nicholson, Andrew C.; Etingin, Orli; Summers, Barbara; Hajjar, David P.
CS Dep. Pathol., Cornell Univ. Med. Coll., NEW YORK, NY, 10021, USA
SO Medical Science Symposia Series (1993), 2(DRUGS AFFECTING LIPID METABOLISM), 251-60
CODEN: MSSYEI; ISSN: 0928-9550
DT Journal; General Review
LA English
AB A review with 21 refs. Calcium channel blockers are now widely used for the **treatment** of hypertension and angina. However, recent evidence suggests that calcium channel blockers may also be beneficial in controlling processes leading to **atherosclerosis**. In these studies, the authors evaluated the effects of two dihydropyridine calcium channel blockers, Nifedipine and Nicardipine on cholesterol metab. in

aortic smooth muscle cells. Nicardipine increased LDL receptor activity that was paralleled by an increase in the steady state level of LDL receptor mRNA. These calcium channel blockers also increased lysosomal and cytoplasmic **cholesteryl ester hydrolase** activities, but did not alter ACAT activity. Since the authors have demonstrated that these processes are modulated by prostacyclin (PGI2) and cAMP, the authors evaluated the effects of calcium channel blockers on PGI2 release and cAMP levels. The authors found that these agents increased both PGI2 release and cAMP prodn. Finally, several calcium channel blockers reduced cholesterol content in cholesterol-enriched smooth muscle cells derived from atherosclerotic rabbits, and reduced cholesterol content in aortic biopsies taken from patients undergoing coronary bypass surgery. Taken together, the authors' data demonstrate that calcium channel blockers reduce cholesterol content in vascular tissue by stimulating LDL catabolism through a process that is mediated by PGI2 and cAMP. The authors' results engender support for the use of calcium channel blockers as anti-atherosclerotic agents.

L11 ANSWER 31 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1987:433633 CAPLUS
DN 107:33633
TI Cholesterol ester synthetase and neutral hydrolase activities of aortic wall in diabetic rat; effects of insulin treatment
AU Onuma, Tomio; Tsutsui, Masahiro; Ochiai, Sigeru; Boku, Akitoshi; Yanada, Atsuko; Takebe, Kazuo
CS Sch. Med., Hirosaki Univ., Hirosaki, 036, Japan
SO Domyaku Koka (1987), 14(6), 1283-6
CODEN: DOMKDM; ISSN: 0386-2682
DT Journal
LA Japanese
AB The effects of diabetes mellitus and of insulin **treatment** on cholesterol ester synthetase (CES) and neutral **cholesterol ester hydrolase** (CEH) activities in rat aortic wall were examd. Male Wistar-King rats were divided into 3 groups; control (C), streptozotocin-induced diabetic (SD), and insulin-**treated** diabetic (ID). CES activity in SD rats was significantly lower than that in ID rats and was slightly lower than in C rats. Neutral CEH activity was slightly low in SD rats and in ID rats, as compared with controls. The ratio of CES activity to neutral CEH activity in SD rats was 50% of that in ID rats and was 66% that in C rats, although the differences were not significant. These results suggest that the decreased risk of **atherosclerosis** in exptl. diabetic animals may be increased by being **treated** insulin.

L11 ANSWER 32 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1986:545991 CAPLUS
DN 105:145991
TI Effects of elastase on experimental atherosclerosis in rabbits
AU Miyaka, Yoshimasa; Shibata, Kaeko; Ito, Toshiko
CS Fac. Pharm., Kinki Univ., Higashi-Osaka, Japan
SO Domyaku Koka (1986), 13(6), 1513-18
CODEN: DOMKDM; ISSN: 0386-2682
DT Journal
LA Japanese
AB In rabbits with **atherosclerosis** induced by the ingestion of 1% cholesterol [57-88-5] in the diet, **treatment** with elastase [9004-06-2] (100 mg/kg/day; 96.2 units/mg) decreased free and very-low-d.-lipoprotein- and low-d.-lipoprotein-assocd. cholesterol levels in the plasma, increased apoprotein A and E, and decreased the activity of **cholesterol esterase** [9026-00-0] and succinyltrialanine-p-nitroanalide hydrolase [72855-17-5] in comparison with the non-drug-**treated** controls. Histopathol. changes in the atheromatous lesions were also diminished by elastase **treatment**.

L11 ANSWER 33 OF 68 CAPLUS COPYRIGHT 2003 ACS

AN 1984:448493 CAPLUS
DN 101:48493
TI Influence of hypocholesterolemic drugs on aortic cholesterol esterase in rabbits
AU Kritchevsky, David; Singer, Deborah; Klurfeld, David M.
CS Wistar Inst. Anat. Biol., Philadelphia, PA, 19104, USA
SO Pharmacological Research Communications (1984), 16(6), 525-31
CODEN: PLRCAT; ISSN: 0031-6989
DT Journal
LA English
AB The influence of 3 hypocholesterolemic drugs (Fenofibrate [49562-28-9], Pirinixil [65089-17-0], and Probucol [23288-49-5]) on aortic **cholesterol esterase** (EC 3.1.1.13) [9026-00-0] activity in cholesterol-fed rabbits was studied. After 3 wk, cholesterol-fed controls exhibited a 28% increase in cholesteryl ester synthetase activity (S) and a 13% decrease in **cholesteryl ester hydrolase** activity (H) giving a 47% increase in S/H ratio. None of the drugs influenced cholesterol-induced synthetase activity, but fenofibrate **treatment** increased hydrolase activity resulting in a fall in the S/H ratio to the level obsd. in rabbits fed corn oil but no cholesterol. The other two hypocholesterolemic agents did not affect the aortic S/H ratio. The relation of these results to the induction of **atherosclerosis** is discussed.

L11 ANSWER 34 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1981:13745 CAPLUS
DN 94:13745
TI Hemodynamic effects on aortic enzyme activities in spontaneously hypertensive rats
AU Tomita, T.; Shirasaki, Y.; Takiguchi, Y.; Ozaki, Y.; Hayashi, E.
CS Dep. Pharmacol., Shizuoka Coll. Pharm. Sci., Shizuoka, 422, Japan
SO Atherosclerosis (Shannon, Ireland) (1980), 37(3), 409-22
CODEN: ATHSBL; ISSN: 0021-9150
DT Journal
LA English
AB Spontaneously hypertensive rats (SHRSP and SHR) and normotensive rats (WKR) were **treated** with hypotensive drugs, and arterial and venous enzyme activities were compared between the **treated** and nontreated hypertensive groups. With the 4 mo expt., **cholesterol esterase** activity in the aorta from hypertensive SHRSP and SHR was significantly lower than that in the resp. **treated** groups, whereas venous activity did not differ. By contrast, aortic N-acetyl-.beta.-D-glucosaminidase activity was significantly higher in the hypertensive groups without any changes in venous activity. Acid phosphatase activity was unaltered. No effects of **treatment** were obsd. in the normotensive WKR. Accompanying a decrease in aortic **cholesterol esterase**, there was a marked increase in aortic cholesteryl esters accompanying hypertension. Aortic phosphodiesterase activity was significantly elevated in the hypertensive SHRSP and SHR compared with the resp. **treated** groups. Thus, hypertension of long duration specifically decreased aortic **cholesterol esterase** activity with a consequent accumulation of cholesteryl esters in the aorta, and this hemodynamic effect seemed to be partly mediated by cAMP with an effect on the lysosomal membrane. These results could provide the biochem. bases for the relation between hypertension and **atherosclerosis**.

L11 ANSWER 35 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1978:473859 CAPLUS
DN 89:73859
TI Baboons and regression
AU Howard, A. N.
CS Dep. Med., Univ. Cambridge, Cambridge, UK
SO Atheroscler. - Is It Reversible? (1978), 57-60. Editor(s): Schettler, Friedrich Gotthard; Stange, Eduard Friedrich; Wissler, Robert William.

Publisher: Springer, Berlin, Ger.
CODEN: 38JLA7
DT Conference
LA English
AB Baboons were given an atherogenic diet and bovine serum albumin i.v. to produce **atherosclerosis**. Concurrent polyunsatd. phosphatidylcholine (I) inhibited the process without greatly affecting serum cholesterol level. In rabbits with the same **treatment** the I increased **cholesterol ester hydrolase** in the aortic wall by 50%. In another expt. baboons were fed an atherogenic diet for 12-16 wk. Then, **treatment** with i.v. I had no effect on the **atherosclerosis**. Atherosclerotic baboons showed increased activity of cholesterol acyltransferase and I decreased this activity.

L11 ANSWER 36 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1977:565662 CAPLUS
DN 87:165662
TI Lipid composition and enzyme activities of human arteriosclerotic femoral and iliac arteries
AU Patelski, J.; Pniewska-Plotast, B.; Majewski, W.; Zapalski, S.
CS Dep. Biochem., Med. Acad., Poznan, Pol.
SO Enzyme (1977), 22(6), 412-15
CODEN: ENZYBT; ISSN: 0013-9432
DT Journal
LA English
AB Lipid compn. and the activities of lipolytic enzymes and cholesterol acyltransferase have been examd. in femoral and iliac arteries of surgically **treated** patients suffering from **arteriosclerosis** obliterans. Neg. correlations for the contents of triglycerides and cholesterol esters, and for the ratios of triglyceride/cholesterol ester contents and cholesterol acyltransferase/ **cholesterol esterase** activities, were found.

L11 ANSWER 37 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1978:16348 CAPLUS
DN 88:16348
TI Effect of estrogens on the activities of cholesteryl ester synthetase and cholesteryl ester hydrolases in pigeon aorta
AU Subbiah, M. T. Ravi
CS Cardiovasc. Res. Unit, Mayo Clin. and Mayo Found., Rochester, MN, USA
SO Steroids (1977), 30(2), 259-65
CODEN: STEDAM; ISSN: 0039-128X
DT Journal
LA English
AB In spontaneously **atherosclerosis**-susceptible pigeons, estrogens decreased the activity of cholesteryl ester synthetase [9027-63-8] and increased the **cholesteryl ester hydrolase** [9026-00-0] activity in the microsomal fraction of the aorta. There was no effect on the **cholesteryl ester hydrolase** activity in the supernatant fraction. The inhibition of cholesteryl ester synthetase and the stimulation of **cholesteryl ester hydrolase** might be responsible for the decreased content of cholesteryl esters noted in pigeon aorta after estrogen **treatment** .

L11 ANSWER 38 OF 68 CAPLUS COPYRIGHT 2003 ACS
AN 1973:427273 CAPLUS
DN 79:27273
TI Effect of intravenous polyunsaturated phosphatidyl choline in experimental atherosclerosis
AU Howard, A. N.; Patelski, J.
CS Dep. Invest. Med., Univ. Cambridge, Cambridge, UK
SO Verhandlungen der Deutschen Gesellschaft fuer Innere Medizin (1972), 78, 1245-8
CODEN: VDGIA2; ISSN: 0070-4067

DT Journal
LA English
AB In rabbits fed an atherogenic diet for 18 weeks, **treatment** with polyunsaturated phosphatidyl choline every 2 days i.v. prevented the increase in phospholipase A [9043-29-2] and lipase [9001-62-1] activities and the decrease in **cholesterol esterase** [9026-00-0] activity. In baboons with exptl. aortic **atherosclerosis**, **treatment** with polyunsatd. soya lecithin i.v. decreased the aortic **atherosclerosis**, normalized the aortic lipase levels, but increased **cholesterol esterase** activity. The increase in plasma cholesterol [57-88-5] obsd. in both atherosclerotic rabbits and baboons was unaffected by polyunsaturated phosphatidyl choline.

L11 ANSWER 39 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 94379101 EMBASE
DN 1994379101
TI Calcium channel blockers and coronary atherosclerosis: From the rabbit to the real world.
AU Waters D.; Lesperance J.
CS Division of Cardiology, Hartford Hospital, 80 Seymour Street,Hartford, CT 06102-5037, United States
SO American Heart Journal, (1994) 128/6 II SUPPL. (1309-1316).
ISSN: 0002-8703 CODEN: AHJOA2
CY United States
DT Journal; Conference Article
FS 005 General Pathology and Pathological Anatomy
014 Radiology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LA English
SL English
AB Many calcium channel blockers have been shown to retard the development of **atherosclerosis** in cholesterol-fed rabbits. The mechanisms that may contribute to this effect include stimulation of **cholesteryl ester hydrolase** activity in smooth muscle cells, amelioration of hypercholesterolemic-induced endothelial dysfunction, or inhibition of smooth muscle cell proliferation and migration. The effect of calcium channel blockers on the evolution of coronary **atherosclerosis** in humans has been assessed in three clinical trials. In the Montreal Heart Institute trial, nicardipine did not influence the overall rate of progression and regression; however, patients **treated** with nicardipine experienced significantly less progression of minimal lesions, defined as stenoses of less than or equal to 20% severity. In the International Nifedipine Trial on Antiatherosclerotic **Therapy** (INTACT), nifedipine had no effect on overall progression and regression but, by one method of analysis, reduced the rate of appearance of new coronary lesions. In a preliminary report, diltiazem prevented the development of coronary **atherosclerosis** in heart transplant recipients. These studies indicate that calcium channel blockers retard the development of early **atherosclerosis** not only in animal models but also in human coronary arteries. Other studies recently completed or now under way will help to clarify the clinical role of calcium channel blockers in antiatherosclerotic **therapy**.

L11 ANSWER 40 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 92173461 EMBASE
DN 1992173461
TI Acid cholesteryl ester hydralase activity of mononuclear leukocytes in patients with non-insulin-dependent diabetes mellitus: Studies before and after treatment of diabetes.
AU Onuma T.; Tsutsui M.; Boku A.; Yanada A.; Ochiai S.; Takebe K.
CS Third Dept. of Internal Medicine, Hirosaki Univ. School of Medicine,Hirosaki 036, Japan
SO Atherosclerosis, (1992) 92/2-3 (229-232).

ISSN: 0021-9150 CODEN: ATHSBL
CY Ireland
DT Journal; Article
FS 003 Endocrinology
006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LA English
SL English
AB The change of acid **cholesteryl ester hydrolase** activity in mononuclear leukocyte following **treatment** of diabetes mellitus was studied in 21 patients with non-insulin-dependent diabetes mellitus (NIDDM). Enzyme activity before **treatment** in the patients was significantly lower than that in 14 age-matched healthy subjects (1.20 .+-. 0.15; mean .+-. S.E. vs. 2.20 .+-. 0.17 nmol/mg protein/h, P < 0.01). Enzyme activity before **treatment** in the patients was significantly increased (P < 0.05) after 4-8 weeks of **treatment**. However, enzyme activity of 1.43 .+-. 0.14 nmol/mg protein/b observed after **treatment** in the patients was significantly lower (P < 0.01) than that in the healthy subjects. There was a significant negative correlation between enzyme activity before **treatment** and the increase in enzyme activity following **treatment** (rs = -0.555, P < 0.01, n = 21). These results indicate that low level of enzyme activity may be insufficiently improved by the **treatment** of diabetes, and the risk for the development of **atherosclerosis** as viewed from the enzyme activity may persist even after the **treatment** in NIDDM.

L11 ANSWER 41 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 92363115 EMBASE
DN 1992363115
TI Interventions that beneficially influence the evolution of coronary atherosclerosis: The case for calcium channel blockers.
AU Waters D.; Lesperance J.
CS Research Centre, Montreal Heart Institute, 5000 East, Belanger Street,Montreal, Que. H1T 1C8, Canada
SO Circulation, (1992) 86/6 SUPPL. (III111-III116).
ISSN: 0009-7322 CODEN: CIRCAZ
CY United States
DT Journal; Conference Article
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Calcium channel blockers have been shown to retard the development of **atherosclerosis** in rabbits fed cholesterol-rich diets. The mechanism accounting for this effect is controversial but may be by stimulation of **cholesteryl ester hydrolase** activity in smooth muscle cells, by amelioration of hypercholesterolemia-induced endothelial dysfunction, or by inhibition of smooth muscle cell proliferation and migration. The effect of calcium channel blockers on the evolution of coronary **atherosclerosis** in humans has been assessed in two clinical trials. In the Montreal Heart Institute trial, nicardipine did not influence the overall rate of progression and regression; however, nicardipine-**treated** patients experienced significantly less progression of minimal lesions, defined as stenoses of .ltoreq.20% severity. In the International Nifedipine Trial on Antiatherosclerotic **Therapy**, nifedipine had no effect on overall progression and regression but reduced the rate of appearance of new coronary lesions. These studies constitute a potentially important new approach to the management of coronary **atherosclerosis**.

L11 ANSWER 42 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 87210398 EMBASE

DN 1987210398
TI Cholestyramine treatment in early life of low-density lipoprotein receptor deficient Watanabe rabbits: Decreased aortic cholesteryl ester accumulation and atherosclerosis in adult life.
AU Subbiah M.T.R.; Yunker R.L.; Rymaszewski Z.; Kottke B.A.; Bale L.K.
CS University Hospital, Mail Location 540, Cincinnati, OH 45267, United States
SO Biochimica et Biophysica Acta - Lipids and Lipid Metabolism, (1987) 920/3 (251-258).
ISSN: 0005-2760 CODEN: BBLLA6
CY Netherlands
DT Journal
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
029 Clinical Biochemistry
030 Pharmacology
LA English
AB Effect of cholestyramine **treatment** in early life of Watanabe heritable hyperlipidemic rabbits (an animal model lacking low-density lipoprotein receptor activity) on subsequent (6 months recovery) occurrence of natural atherosclerotic lesion and arterial cholesterol metabolism was investigated. Initial cholestyramine **treatment** decreased both plasma total cholesterol and HDL-cholesterol levels which normalized within 4 weeks after **treatment** was discontinued. At 9 months of age (age of occurrence of spontaneous atherosclerotic lesions), the extent of aortic **atherosclerosis** in cholestyramine pre-**treated** animals was modestly lower ($P < 0.05$), as compared to controls, with a significant ($P < 0.05$) decrease in aortic cholesteryl ester content. Furthermore, at the end of the recovery period aortic activity of acyl-CoA:cholesterol acyltransferase and neutral **cholesterol esterase** activity was significantly ($P < 0.05$) lower in cholestyramine-pretreated animals. These studies show that early cholestyramine pre-**treatment** in a low-density lipoprotein receptor-deficient animal model causes persistent changes which might influence cholesteryl ester accumulation and atherogenesis in adult life, even after cholestyramine **treatment** is discontinued.

L11 ANSWER 43 OF 68 MEDLINE
AN 90342015 MEDLINE
DN 90342015 PubMed ID: 2382265
TI Acid cholesteryl ester hydrolase activity of mononuclear leukocyte in type 2 (non-insulin-dependent) diabetic patients.
AU Onuma T; Tsutsui M; Ochiai S; Boku A; Yanada A; Hirai Y; Nakahata H; Takebe K
CS Third Department of Internal Medicine, Hirosaki University School of Medicine.
SO TOHOKU JOURNAL OF EXPERIMENTAL MEDICINE, (1990 Apr) 160 (4) 375-81.
Journal code: 0417355. ISSN: 0040-8727.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199009
ED Entered STN: 19901012
Last Updated on STN: 19901012
Entered Medline: 19900912
AB Acid **cholesteryl ester hydrolase** activity of mononuclear leukocytes was measured in 52 Type 2 (non-insulin-dependent) diabetic patients. Enzyme activity was significantly lower in the diabetic patients than in 14 age-matched control subjects (0.89 +/- 0.08 (mean +/- S.E.) vs. 2.20 +/- 0.17 nmol/mg protein/hr, p less than 0.01). In diabetic patients undergoing diet **treatment** only, the enzyme activity was significantly lower in poorly controlled patients than in well controlled patients (0.43 +/- 0.03 vs. 1.15 +/- 0.24 nmol/mg protein/hr, p less than 0.01). In the diabetic patients, there was a significant negative

correlation between the enzyme activity and serum total cholesterol or low density lipoprotein cholesterol level (r = -0.361, p less than 0.01, n = 52 or r = -0.630, p less than 0.01, n = 28). These results suggest that a low level of acid **cholesteryl ester hydrolase** activity in mononuclear leukocyte might play an important role in the progression of **atherosclerosis** in Type 2 diabetes.

L11 ANSWER 44 OF 68 MEDLINE
AN 80142369 MEDLINE
DN 80142369 PubMed ID: 7360009
TI The effect of oral contraceptives on mononuclear cell cholesteryl ester hydrolase activity.
AU Hagemenas F C; Yatsu F M; Manaugh L C
SO LIPIDS, (1980 Jan) 15 (1) 39-44.
Journal code: 0060450. ISSN: 0024-4201.
Report No.: PIP-800895; POP-00078288.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Population
EM 198005
ED Entered STN: 19900315
Last Updated on STN: 20021101
Entered Medline: 19800514
AB The influence of sex steroids on mononuclear cell **cholesteryl ester hydrolase** (CEH) activity in premenopausal women and women on combined estrogen-progestin oral contraceptives has been studied. In addition, plasma and mononuclear cell cholesterol and esters were measured along with plasma estrogen and progesterone levels. Mononuclear cell CEH activity in control women is highest on Day 20 of their menstrual cycle. The control women had significantly higher CEH activities than women on oral contraceptives. Plasma esters were higher in the oral contraceptive group. However, in mononuclear cells, free cholesterol but not cholesteryl esters were higher in women on oral contraceptives.
Premenopausal women, 1 control group (n=9) taking no medication or using no oral contraceptives (OCs) and 1 **treated** group (n=10) receiving OCs for contraception, were studied to determine any effects OCs have on mononuclear cell **cholesteryl ester hydrolase** (CEH) activity. 9 of the 10 medicated women were taking Ortho Novum 1/50 and the other person was receiving Norlestrin 1/50. Normally menstruating women (controls) showed a significant rise in CEH levels on Day 20 of the menstrual cycle (P .05). The enzyme activity in women on OCs was significantly lower than control women in 3 of 4 testing periods. In addition, plasma and mononuclear cell cholesterol and esters were measured along with plasma estrogen and progesterone levels. Although free cholesterol levels in normal cycling (control) women and in the OC group did not vary significantly during the menstrual cycle between the 2 groups, the women on OCs had significantly higher ester levels than the control women in 3 of the 4 test periods P .05-.005). When paired ratios of plasma cholesterol to esterified cholesterol were compared between control and OC groups, the ratio of free/esterified was significantly higher in the control group in 3 of 4 tests. In the mononuclear cells, on the other hand, the cholesterol/cholesteryl ester ratio was significantly lower in the control group during the 4 test periods. No association between levels of endogenous sex hormones (estradiol, progesterone) and CEH activity were found. CEH levels may be related to incidence of **atherosclerosis**, and women taking OCs may have increased chances of developing this disease.

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